89446

Access DB#

SEARCH REQUEST FORM

Scientific and Technical Information Center

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Requester's Full Name: Jeff	ZE. Russel	Examiner # :_	62785 Date: 3	-19-20d3
	Number 308-397		ımber: <u>10/018,87°</u>	
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Please provide a detailed statement of th Include the elected species or structures, utility of the invention. Define any term known. Please attach a copy of the cover	keywords, synonyms, ac is that may have a special	cronyms, and registry and meaning. Give exam	numbers, and combine wi	th the concept or
Title of Invention: Amphiphilic	Dry-Oligoner	Conjugados Wit	2 Mydroly zable Lipop	Lile Components
Inventors (please provide full names):	N. Etworibe,	M. Ramaswa	My J. Rajago	palan :
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Searcher Location:	Structure (#)	Questel/Orbit		
Date Searcher Picked Up: 3/20/03	Bibliographic	Dr.Link		
Date Completed: 4/1d03	Litigation			
Searcher Prep & Review Time: 60	Fulltext			•
Clerical Prep Time:	•	•		
Te	Patent Family			
Online Time: / 3	Other	Other (specify)		
PTO-1590 (8-01)	į			

Russel 09/018,879

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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> fil hcaplu FILE 'HCAPLUS' ENTERED AT 15:35:11 ON 10 APR 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 10 Apr 2003 VOL 138 ISS 15 FILE LAST UPDATED: 9 Apr 2003 (20030409/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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STR
L1
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    0
CH2-C-\(\sigma\) O-\(\sigma\) CH2-CH2-O-\(\sigma\) CH2-CH2
  2 3 4 5 6 7
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS
STEREO ATTRIBUTES: NONE
            6984) SEA FILE=REGISTRY SSS FUL L1
L2
    (
           10066) SEA FILE=HCAPLUS L2
L3
    (
              89 SEA FILE=HCAPLUS L3 (L) (CONJUG? OR PROTEIN? OR ?PEPTIDE? OR
T.4
                 ?INSULIN?)
                 STR
L5
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O CH2·CH2·O~~ CH2·C~~ O~~ CH2·CH2 1 2 3 4 5 6 7 8

9

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

Page 2 09/018,879 Russel

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

813 SEA FILE=REGISTRY SSS FUL L5 L6

L.7 STR

11

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DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

406 SEA FILE=REGISTRY SSS FUL L7 r_8

570 SEA FILE=HCAPLUS L6 L9360 SEA FILE=HCAPLUS L8 L10

6543 SEA FILE=REGISTRY INSULIN/BI L12 155255 SEA FILE=HCAPLUS L12 OR INSULIN L13

32181 SEA FILE=HCAPLUS CONJUG? (L) (PROTEIN? OR ?PEPTIDE? OR L13) L14

30 SEA FILE=HCAPLUS L14 AND (L4 OR L9 OR L10) L15

=> d ibib abs hitrn 115 1-30

L15 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2002:946130 HCAPLUS

DOCUMENT NUMBER:

138:29120

TITLE:

Preparation of peptide drug-alkylene glycol

oligomer conjugates

INVENTOR(S):

Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari,

Aslam M.; Odenbaugh, Amy L.

PATENT ASSIGNEE(S):

SOURCE:

Nobex Corporation, USA PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. ______ ______ WO 2002098446 A1 20021212 WO 2002-US17567 20020604 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,

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TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     BR 2001006401
                            20030211
                                           BR 2001-6401
                       Α
                                                            20011011
     JP 2003104913
                            20030409
                                           JP 2001-317307
                       Α2
                                                             20011015
PRIORITY APPLN. INFO.:
                                        US 2001-873797
                                                         A 20010604
OTHER SOURCE(S):
                         MARPAT 138:29120
     A non-polydispersed mixt. of conjugates in which each
     conjugate in the mixt. comprises a peptide drug coupled
     to an oligomer that includes a polyalkylene glycol moiety is disclosed.
     The mixt. may exhibit higher in vivo activity than a polydispersed mixt.
     of similar conjugates. The mixt. may be more effective at
     surviving an in vitro model of intestinal digestion than polydispersed
     mixts. of similar conjugates. The mixt. may result in less
     inter-subject variability than polydispersed mixts. of similar
     conjugates. Thus, non-polydispersed hexaethylene glycol was
     treated with phosgene soln., followed by treatment with
     N-hydroxysuccinimide (NHS) to give give the NHS ester. Human growth
     hormone (Saizen) was allowed to react with the NHS ester to give the
     conjugate.
     62304-85-2P 70802-40-3P 477775-74-9P
ΙT
     477775-75-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (in alkylene glycol derivs. prepn.; prepn. of peptide
        drug-alkylene glycol oligomer conjugates)
ΙT
     259228-98-3P 477775-76-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of peptide drug-alkylene glycol oligomer
        conjugates)
TΤ
     8049-62-5DP, Zinc insulin, conjugates with
    alkylene glycols 9004-10-8DP, Insulin,
    conjugates with alkylene glycols 11061-68-0DP, Human
     insulin, conjugates with alkylene glycols
     59112-80-0DP, C-Peptide, conjugates with
    alkylene glycols 106602-62-4DP, Amylin, conjugates
    with alkylene glycols 259228-98-3DP, peptide drug
    conjugates 477775-76-1DP, peptide drug
     conjugates
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of peptide drug-alkylene glycol oligomer
        conjugates)
                               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         6
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L15 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2003 ACS
                         2002:946037 HCAPLUS
ACCESSION NUMBER:
                         138:16621
DOCUMENT NUMBER:
                         Preparation of insulin-alkylene glycol
TITLE:
                         oligomer conjugates
                         Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari,
INVENTOR(S):
                         Aslam M.; Odenbaugh, Amy L.; Radhakrishnan, Balasingam
                         Nobex Corporation, USA
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 127 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
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LANGUAGE: English

PATENT INFORMATION:

FAMILY ACC. NUM. COUNT:

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PATENT NO.
                     KIND DATE
                                         APPLICATION NO. DATE
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                                       WO 2002-US17574 20020604
                    A1 20021212
     WO 2002098232
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
            TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2003027748
                     A1 20030206
                                        US 2001-873899 20010604
                                       US 2001-873899
PRIORITY APPLN. INFO.:
                                                       A 20010604
                        MARPAT 138:16621
OTHER SOURCE(S):
    A mixt. of conjugates in which each conjugate in the
    mixt. comprises an insulin drug coupled to an oligomer that
    includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit
    higher in vivo activity than a polydispersed mixt. of similar
    conjugates. The mixt. may also be more effective at surviving an
    in vitro model of intestinal digestion than polydispersed mixts. of
    similar conjugates. The mixt. may also result in less
    inter-subject variability than polydispersed mixts. of similar
    conjugates. Thus, non-polydispersed hexaethylene glycol was
    treated with phosgene soln., followed by treatment with
    N-hydroxysuccinimide (NHS) to give give the NHS ester. Human
    insulin was dissolved in DMSO and allowed to react with the NHS
    ester to give the conjugate.
    62304-85-2P 70802-40-3P 477775-74-9P
ΙT
    477775-75-0P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (in alkylene glycol derivs. prepn.; prepn. of insulin
        -alkylene glycol oligomer conjugates)
    8049-62-5DP, Zinc Insulin, alkylene glycol oligomer
TT
    conjugates 9004-10-8DP, Insulin, alkylene
    glycol oligomer conjugates 11061-68-0DP, Human
    insulin, alkylene glycol oligomer conjugates
    259228-98-3DP, insulin conjugates
    477775-76-1DP, insulin conjugates
    RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (prepn. of insulin-alkylene glycol oligomer
       conjugates)
    259228-98-3P 477775-76-1P
IT
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of insulin-alkylene glycol oligomer
       conjugates)
                              THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

ACCESSION NUMBER: 2002:700064 HCAPLUS

DOCUMENT NUMBER: 138:122793

TITLE: A new and efficient method for synthesis of

5'-conjugates of oligonucleotides through amide-bond

formation on solid phase

AUTHOR(S): Kachalova, Anna V.; Stetsenko, Dmitry A.; Romanova, Elena A.; Tashlitsky, Vadim N.; Gait, Michael J.;

Oretskaya, Tatiana S.

CORPORATE SOURCE: Chemistry Department and A. N. Belozersky Institute of

Physico-Chemical Biology, M. V. Lomonosov Moscow State

University, Moscow, 119992, Russia

SOURCE: Helvetica Chimica Acta (2002), 85(8), 2409-2416

CODEN: HCACAV; ISSN: 0018-019X Verlag Helvetica Chimica Acta

PUBLISHER: Verlag F
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:122793

An efficient method for synthesis of oligonucleotide 5'-conjugates through amide-bond formation on solid phase is described. Protected oligonucleotides contg. a 5'-carboxylic acid function were, obtained by use of a novel non-nucleosidic phosphoramidite building block, where the carboxylic acid moiety was protected by a 2-chlorotrityl group. The protecting group is stable to the phosphoramidite coupling conditions used in solid-phase oligonucleotide assembly, but is easily deprotected by mild acidic treatment. The protecting group may be removed also by ammonolysis. 5'-Carboxylate-modified oligonucleotides were efficiently on solid support under normal peptide-coupling conditions to various amines or to the N-termini of small peptides to yield products of high purity. The method is well-suited in principle for the synthesis of peptide-oligonucleotide conjugates contg. an amide linkage between the 5'-end of an oligonucleotide and the N-terminus of a peptide.

IT 199869-48-2

RL: RCT (Reactant); RACT (Reactant or reagent) (solid phase synthesis of 5'-conjugates of oligonucleotides through amide-bond formation)

REFERENCE COUNT:

THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2002:324975 HCAPLUS

26

DOCUMENT NUMBER:

137:90504

TITLE:

Carbohydrate arrays for the evaluation of protein

binding and enzymatic modification

AUTHOR(S): CORPORATE SOURCE: Houseman, Benjamin T.; Mrksich, Milan

PORATE SOURCE: The Institute for Biophysical Dynamics, Department of

Chemistry, The University of Chicago, Chicago, IL,

60637, USA

SOURCE:

Chemistry & Biology (2002), 9(4), 443-454

CODEN: CBOLE2; ISSN: 1074-5521

PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This paper reports a chem. strategy for prepg. carbohydrate arrays and utilizes these arrays for the characterization of carbohydrate-protein interactions. Carbohydrate chips were prepd. by the Diels-Alder-mediated immobilization of carbohydrate-cyclopentadiene conjugates to self-assembled monolayers that present benzoquinone and penta(ethylene glycol) groups. Surface plasmon resonance spectroscopy

showed that lectins bound specifically to immobilized carbohydrates and that the glycol groups prevented nonspecific protein adsorption. Carbohydrate arrays presenting ten monosaccharides were then evaluated by profiling the binding specificities of several lectins. These arrays were also used to det. the inhibitory concns. of sol. carbohydrates for lectins and to characterize the substrate specificity of .beta.-1,4-galactosyltransferase. Finally, a strategy for prepg. arrays with carbohydrates generated on solid phase is shown. This surface engineering strategy will permit the prepn. and evaluation of carbohydrate arrays that present diverse and complex structures.

IT 154773-34-9P 441775-29-7P 441775-30-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(carbohydrate arrays for evaluation of protein binding and enzymic

modification)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:409049 HCAPLUS

DOCUMENT NUMBER: 135:167010

TITLE: A Convenient Solid-Phase Method for Synthesis of

3'-Conjugates of Oligonucleotides

AUTHOR(S): Stetsenko, Dmitry A.; Gait, Michael J.

CORPORATE SOURCE: Laboratory of Molecular Biology, Medical Research

Council, Cambridge, CB2 2QH, UK

SOURCE: Bioconjugate Chemistry (2001), 12(4), 576-586

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:167010

We present a new procedure for the prepn. of 3'-conjugates of oligonucleotides through solid-phase synthesis. A suitable universal solid support was readily prepd. using a series of peptide-like coupling reactions to incorporate first a spacer and then an L-homoserine branching unit. The N-.alpha.-position of the homoserine carries an Fmoc protecting group that is removed by treatment with piperidine to liberate an amino group suitable for attachment of the conjugate (e.g., small org. mol., fluorescent group, cholesterol, biotin, amino acid, etc.) or for assembly of a short peptide. The side-chain hydroxyl group of the homoserine carries a trityl protecting group. After TFA deprotection, the hydroxyl group acts as the site for oligonucleotide assembly. An addnl. spacer, such as aminohexanoyl, may be incorporated easily between the conjugate mol. and the oligonucleotide. A no. of examples of synthesis of 3'-conjugates of oligonucleotides and their analogs are described that involve std. automated oligonucleotide assembly and use of com. available materials. The linkage between oligonucleotide and 3'-conjugate is chirally pure and is stable to conventional ammonia treatment used for oligonucleotide deprotection and release from the solid support. The homoserine-functionalized solid support system represents a simple and universal route to 3'-conjugates of oligonucleotides and their derivs.

IT 352535-99-0P 352536-02-8DP, controlled pore glass support 352536-04-0DP, controlled pore glass support 352536-10-8DP, controlled pore glass support 352536-12-0DP, controlled pore glass support 352536-14-2DP, controlled pore glass support 353241-41-5DP, controlled pore glass support

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(solid phase synthesis of conjugates of peptide

-contg. oligonucleotides)

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:409048 HCAPLUS

DOCUMENT NUMBER: 135:157549

TITLE: Studies on Protein-Liposome Coupling Using Novel
Thiol-Reactive Coupling Lipids: Influence of Spacer

Length and Polarity

AUTHOR(S): Fleiner, Michael; Benzinger, Petra; Fichert, Thomas;

Massing, Ulrich

CORPORATE SOURCE: Department of Clinical Research, Tumor Biology Center,

Freiburg, D-79106, Germany

SOURCE: Bioconjugate Chemistry (2001), 12(4), 470-475

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

To optimize the prepn. of immunoliposomes, we investigated the coupling of thiolated IgG and BSA to liposomes using a novel group of coupling lipids. All lipids consist of cholesterol as membrane anchor and a thiol-reactive maleimide headgroup, linked by a spacer that differs in length and polarity (ethylene glycol, tetraethylene glycol, PEG 400, PEG 1000, dodecyl). In addn., lipids differ in the electrophilicity of the maleimide group (p- or m-maleimidobenzoic ester). In the case of BSA, coupling efficiency strongly depended on the electrophilicity of the maleimide group as well as on the spacer polarity: the less electrophilic meta constitution seems to be an advantage over the p-maleimidobenzoic ester, resulting in higher coupling efficiency. Polar spacers (tetraethylene glycol, 46%) achieved a higher coupling efficiency than a nonpolar spacer with approx. the same length (dodecyl, 15%). When liposomes contq. coupling lipids with the spacers tetraethylene glycol, PEG 400, and PEG 1000 were linked to BSA, coupling efficiencies were in a medium range and similar (41-46%) but were lower for the short ethylene glycol spacer (30%). In contrast, for IgG coupling efficiencies correlated with increasing spacer length. Best results were obtained using coupling lipids with a long polar spacer (PEG 1000) (65%), whereas a coupling lipid bearing a short spacer (ethylene glycol) resulted in a low coupling efficiency of 12%.

IT 204652-44-8P 204652-45-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(spacer length and polarity effect on protein-liposome

coupling using thiol-reactive coupling lipids)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:255941 HCAPLUS

DOCUMENT NUMBER: 134:266736

TITLE: Soluble, degradable poly(ethylene glycol) derivatives

for controllable release of bound molecules into

solution

INVENTOR(S): Harris, J. Milton

PATENT ASSIGNEE(S): Shearwater Corporation, USA

SOURCE: U.S., 13 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	TENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US	6214966	В1	20010410	US 1997-937846	19970925	
US	2001021763	A1	20010913	US 2001-824297	20010402	
US	6515100	В2	20030204			

PRIORITY APPLN. INFO.: US 1996-26716P P 19960926 US 1997-937846 A3 19970925

AB PEG and related polymer derivs. having weak, hydrolytically unstable linkages near the reactive end of the polymer are provided for conjugation to drugs, including proteins, enzymes, small mols., and others. These derivs. provide a sufficient circulation period for a drug-PEG conjugate and then for hydrolytic breakdown of the conjugate and release of the bound mol. In some cases, drugs that previously had reduced activity when permanently coupled to PEG can have therapeutically suitable activity when coupled to a degradable PEG in accordance with the invention. The PEG of the invention can be used to impart water soly., size, slow rate of kidney clearance, and reduced immunogenicity to the conjugate. Controlled hydrolytic release of the bound mol. in the aq. environment can then enhance the drug delivery system. Polyethylene glycol Me 2-(2pyridyldithio) ethoxycarbonylmethyl ether was prepd. and the hydrolytic half-life of the ester linkage detd.

331968-66-2P 331968-70-8P 331968-74-2P 331968-77-5P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(sol., degradable polyethylene glycol derivs. for controllable release of bound mols. into soln.)

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: . 12 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2000:911065 HCAPLUS

DOCUMENT NUMBER:

134:76386

TITLE:

Amphiphilic drug-oligomer conjugates with hydrolyzable

lipophile components and methods for making and using

INVENTOR(S):

Ekwuribe, Nnochiri; Ramaswamy, Muthukumar;

Rajagopalan, Jayanthi

PATENT ASSIGNEE(S):

Protein Delivery, Inc., USA

SOURCE:

PCT Int. Appl., 69 pp.

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078302	Δ1	20001228	WO 2000-US16879	20000619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,

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HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
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             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
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             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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                            20020402
                                           BR 2000-11772
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                                                             20000619
     EP 1196157
                            20020417
                                           EP 2000-942956
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                                                             20000619
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2003502364
                       T2
                                            JP 2001-504366
                            20030121
                                                             20000619
     NO 2001006143
                       Α
                            20020218
                                            NO 2001-6143
                                                             20011217
PRIORITY APPLN. INFO.:
                                         US 1999-336548
                                                          Α
                                                             19990619
                                        WO 2000-US16879 W 20000619
AB
     The present invention relates generally to hydrolyzable drug-oligomer
     conjugates, pharmaceutical compns. comprising such
     conjugates, and to methods for making and using such
     conjugates and pharmaceutical compns. For example, a
     conjugate of insulin, PEG, and oleic acid was prepd. and
     can be orally administered.
ΤТ
     59392-49-3, Gastric inhibitory peptide
     61912-98-9, Insulin-like growth factor
     67763-96-6, Insulin-like growth factor I
     67763-97-7, Insulin-like growth factor II
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (amphiphilic drug-oligomer conjugates with hydrolyzable
        lipophile components)
ΙT
     9004-10-8, Insulin, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (amphiphilic drug-oligomer conjugates with hydrolyzable
        lipophile components)
IT
     10233-14-4P, Triethylene glycol oleate
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (amphiphilic drug-oligomer conjugates with hydrolyzable
        lipophile components)
     9004-10-8DP, Insulin, conjugates with PEG
ΙT
     derivs., biological studies 10233-14-4DP, Triethylene glycol
     oleate, conjugates with insulin 28397-10-6DP
     , Octanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester,
     conjugates with insulin 62304-85-2DP,
     Hexadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester,
     conjugates with insulin
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (amphiphilic drug-oligomer conjugates with hydrolyzable
        lipophile components)
                               THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         11
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L15 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2003 ACS
                         2000:788342
ACCESSION NUMBER:
                                      HCAPLUS
                         134:136545
DOCUMENT NUMBER:
                         Design of folic acid-conjugated nanoparticles for drug
TITLE:
                         targeting
                         Stella, Barbara; Arpicco, Silvia; Peracchia, Maria
AUTHOR(S):
```

Teresa; Desmaele, Didier; Hoebeke, Johan; Renoir, Michel; D'Angelo, Jean; Cattel, Luigi; Couvreur,

Patrick

CORPORATE SOURCE: Universite Paris-Sud XI, Physico-Chimie-

Pharmacotechnie-Biopharmacie, UMR CNRS 8612-5,

Chatenay-Malabry, 92296, Fr.

SOURCE: Journal of Pharmaceutical Sciences (2000), 89(11),

1452-1464

CODEN: JPMSAE; ISSN: 0022-3549

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: LANGUAGE:

Journal English

The new concept developed in this study is the design of poly(ethylene glycol) (PEG)-coated biodegradable nanoparticles coupled to folic acid to target the folate-binding protein; this mol. is the sol. form of the folate receptor that is overexpressed on the surface of many tumoral cells. For this purpose, a novel copolymer, the poly[aminopoly(ethylene glycol)cyanoacrylate-co-hexadecyl cyanoacrylate] [poly(H2NPEGCA-co-HDCA)] was synthesized and characterized. Then nanoparticles were prepd. by nanopptn. of the obtained copolymer, and their size, zeta potential, and surface hydrophobicity were investigated. Nanoparticles were then conjugated to the activated folic acid via PEG terminal amino groups and purified from unreacted products. Finally, the specific interaction between the conjugate folate-nanoparticles and the folate-binding protein was evaluated by surface plasmon resonance. This anal. confirmed a specific binding of the folate-nanoparticles to the folate-binding protein. This interaction did not occur with nonconjugated nanoparticles used as control. Thus, folate-linked nanoparticles represent a potential new drug

IT 321905-00-4DP, deprotected

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(design of folic acid-conjugated nanoparticles for drug targeting)

IT 321904-99-8P 321905-00-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(design of folic acid-conjugated nanoparticles for drug

targeting)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2003 ACS

carrier for tumor cell-selective targeting.

ACCESSION NUMBER:

2000:755211 HCAPLUS

DOCUMENT NUMBER:

133:340208

TITLE:

SOURCE:

Novel compositions useful for delivering

anti-inflammatory agents into a cell Unger, Evan C.; McCreery, Thomas; Sadewasser, David A.

INVENTOR(S):

ImaRx Pharmaceutical Corp., USA

PATENT ASSIGNEE(S):

Eur. Pat. Appl., 78 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

PRIORITY APPLN. INFO.:

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    EP 1046394 A2 20001025
EP 1046394 A3 20011010
                                          EP 2000-303249
                                                           20000418
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.:
                                       US 1999-294623
                                                        A 19990419
    The present invention is directed, inter alia, to compns. and their use
     for delivering compds. into a cell. In a preferred embodiment, the
     compns. comprise, in combination with the compd. to be delivered, an org.
     halide, a targeting ligand, and a nuclear localization sequence,
     optionally in the presence of a carrier. Ultrasound may be applied, if
     desired. The compns. are particularly suitable for the treatment of
     inflammatory diseases.
    303096-39-1P 303096-53-9P
ΙT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (peptide compns. useful for delivering anti-inflammatory
        agents into a cell)
IT
    303096-30-2P
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
    study); PREP (Preparation); USES (Uses)
        (peptide compns. useful for delivering anti-inflammatory
        agents into a cell)
    ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
                     - 2000:133428 HCAPLUS
DOCUMENT NUMBER:
                        132:185416
TITLE:
                        Blood-brain barrier therapeutics
INVENTOR(S):
                        Ekwuribe, Nnochiri N.; Radhakrishnan, Balasingam;
                        Price, Christopher H.; Anderson, Wesley R., Jr.;
                        Ausari, Aslam M.
PATENT ASSIGNEE(S):
                        Protein Delivery, Inc., USA
SOURCE:
                        PCT Int. Appl., 75 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
                        English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                    KIND DATE
                                        APPLICATION NO. DATE
    PATENT NO.
                     ____
                                          _____
    WO 2000009073
                    A2
                           20000224
                                         WO 1999-US18248 19990812
                     A3 20000629
    WO 2000009073
            AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
            KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
            NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
            UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
            ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
            CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                        CA 1999-2340418 19990812
                     AA 20000224
    CA 2340418
                           20000306
                                         AU 1999-56726
                                                           19990812
    AU 9956726
                      A1
                      A2
                           20010613
                                         EP 1999-943676
                                                           19990812
    EP 1105142
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
                                          BR 1999-14280
                                                           19990812
    BR 9914280
                    Α
                           20011113
                                          JP 2000-564577
                                                           19990812
                      T2
                           20020723
    JP 2002522463
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US 1998-134803 A 19980814

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WO 1999-US18248 W 19990812
AB
     The present invention relates to amphiphilic drug-oligomer
     conjugates capable of traversing the blood-brain barrier and to
     methods of making and using such conjugates. Amphiphilic
     drug-oligomer conjugates comprise a therapeutic compd.
     conjugated to an oligomer, wherein the oligomer comprises a
     lipophilic moiety coupled to a hydrophilic moiety. The conjugates
     of the invention further comprise therapeutic agents such as
     proteins, peptides, nucleosides, nucleotides, antiviral
     agents, antineoplastic agents, antibiotics, etc., and prodrugs,
     precursors, derivs. and intermediates thereof, chem. coupled to
     amphiphilic oligomers. One example conjugate prepd. was
     Met-enkephalin with a succinimidyl triethylene glycol monohexadecyl ester
     deriv.
     9004-10-8DP, Insulin, conjugates with
     polyoxyalkylene deriv., biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); PROC (Process); USES (Uses)
        (blood-brain barrier therapeutics comprising drug-oligomer
        conjugates)
ΙT
     62304-85-2P, Triethylene glycol monohexadecanoate
     259228-98-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (blood-brain barrier therapeutics comprising drug-oligomer
        conjugates)
     62304-85-2DP, conjugates with enkephalin
TΤ
     259229-01-1DP, conjugates with enkephalin
     259229-02-2DP, conjugates with enkephalin
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (blood-brain barrier therapeutics comprising drug-oligomer
        conjugates)
ΙT
     259229-07-7 259229-08-8
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (blood-brain barrier therapeutics comprising drug-oligomer
        conjugates)
L15 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2003 ACS
                         2000:81382 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         132:251326
                         Synthesis of end-labeled multivalent ligands for
TITLE:
                         exploring cell-surface-receptor-ligand interactions
                         Gordon, Eva J.; Gestwicki, Jason E.; Strong, Laura E.;
AUTHOR(S):
                         Kiessling, Laura L.
                         Departments of Chemistry and Biochemistry, University
CORPORATE SOURCE:
                         of Wisconsin-Madison, Madison, WI, 53706, USA
                         Chemistry & Biology (2000), 7(1), 9-16
SOURCE:
                         CODEN: CBOLE2; ISSN: 1074-5521
                         Elsevier Science Ltd.
PUBLISHER:
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
OTHER SOURCE(S):
                         CASREACT 132:251326
    Background: Ring-opening metathesis polymn. (ROMP) is a powerful synthetic
    method for generating unique materials. The functional group tolerance of
    ruthenium ROMP initiators allows the synthesis of a wide range of biol.
    active polymers. We generated multivalent ligands that inhibit cell
    surface L-selectin, a protein that mediates lymphocyte homing
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and leukocyte recruitment in inflammation. We hypothesized that these ligands function through specific, multivalent binding to L-selectin. To examine this and to develop a general method for synthesizing multivalent materials with end-labels, we investigated functionalized enol ethers as capping agents in ruthenium-initiated ROMP. Results: We synthesized a bifunctional mol. that introduces a unique end group by terminating ruthenium-initiated ROMP reactions. This agent contains an enol ether at one end and a masked carboxylic acid at the other. We conjugated a fluorescein deriv. to an end-capped neoglycopolymer that had previously been shown to inhibit L-selectin function. We used fluorescence microscopy to visualize neoglycopolymer binding to cells displaying L-selectin. Our results suggest that the neoglycopolymers bind specifically to cell surface L-selectin through multivalent interactions. Conclusions: Ruthenium-initiated ROMP can be used to generate biol. active, multivalent ligands terminated with a latent functional group. The functionalized polymers can be labeled with a variety of mol. tags, including fluorescent mols., biotin, lipids or antibodies. The ability to conjugate reporter groups to ROMP polymers using this strategy has broad applications in the material and biol. sciences.

IT 262857-77-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of end-labeled multivalent ligands fluorescein neoglycopolymer for exploring cell-surface-receptor-ligand interactions)

REFERENCE COUNT:

THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1999:484864 HCAPLUS

DOCUMENT NUMBER:

131:272145

TITLE:

Synthesis of Novel GABA Uptake Inhibitors. 3.

Diaryloxime and Diarylvinyl Ether Derivatives of Nipecotic Acid and Guvacine as Anticonvulsant Agents Knutsen, Lars J. S.; Andersen, Knud Erik; Lau, Jesper;

AUTHOR(S):

Knutsen, Lars J. S.; Andersen, Knud Erik; Lau, Jesper Lundt, Behrend F.; Henry, Rodger F.; Morton, Howard E.; Nrum, Lars; Petersen, Hans; Stephensen, Henrik; Suzdak, Peter D.; Swedberg, Michael D. B.; Thomsen,

Christian; Sorensen, Per O.

CORPORATE SOURCE:

Health Care Discovery and Development, Novo Nordisk

A/S, Malov, DK-2760, Den.

SOURCE:

Journal of Medicinal Chemistry (1999), 42(18),

3447-3462

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB (3R)-1-[4,4-bis(3-methyl-2-thienyl)-3-butenyl]-3-piperidinecarboxylic acid (tiagabine, Gabitril) is a potent and selective .gamma.-aminobutyric acid (GABA) uptake inhibitor with proven anticonvulsant efficacy in humans. This drug, which has a unique mechanism of action among marketed anticonvulsant agents, has been launched for add-on treatment of partial seizures with or without secondary generalization in patients >12 yr of age. Using this new agent as a benchmark, we have designed two series of novel GABA uptake inhibitors of remarkable potency, using a putative new model of ligand interaction at the GABA transporter type 1 (GAT-1) uptake site. This model involves the postulated interaction of an electroneg. region in the GABA uptake inhibitor with a pos. charged domain in the protein structure of the GAT-1 site. These two novel series of

Russel 09/018,879 .

anticonvulsant agents contain diaryloxime or diarylvinyl ether functionalities linked to cyclic amino acid moieties and were derived utilizing the new model, via a series of design steps from the known 4,4-diarylbutenyl GABA uptake inhibitors. The new compds. are potent inhibitors of [3H]-GABA uptake in rat brain synaptosomes in vitro, and their antiepileptic potential was demonstrated in vivo by their ability to protect against seizures induced by the benzodiazepine receptor inverse agonist Me 4-ethyl-6,7-dimethoxy-.beta.-carboline-3-carboxylate (DMCM) in mice. From structure-activity studies of these new GABA uptake inhibitors, we have shown that insertion of an ether oxygen in conjugation with the double bond in tiagabine (Ki = 67 nM) improves in vitro potency by 5-fold to 14 nM.

IT 131029-43-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of diaryloxime and diarylvinyl ether derivs. of nipecotic acid and guvacine as anticonvulsant agents)

REFERENCE COUNT:

83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1999:460345 HCAPLUS

DOCUMENT NUMBER:

131:88341

TITLE:

Polyamide oligomers and their use in drug delivery via

liposomes

INVENTOR(S):

Ansell, Steven Michial

PATENT ASSIGNEE(S):

Inex Pharmaceuticals Corporation, Can.

SOURCE:

PCT Int. Appl., 106 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

		rent 1													DATE				
		9933					1999					98-C			1998	1222			
		W:	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,	
			DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	
			KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	
															SL,				
				•											KZ,				TM
		RW:	-				-								CY,				
									-		-				вJ,		-	-	
							ML,						•			,	,	•	
	CA	2315											3156	95	1998	1222			
		9917																	
		7514																	
		1041								E	P 19	98-9	6215	8	1998	1222			
															NL,		MC,	PT,	
			IE,		-	·		•	·	•	·		•	·		•		•	
	US	6320			В:	1	2001	1120		U	S 19	98-2	1898	8	19983	1222			
		2001													19983	1222			
		2002													20010	0830			
PRIC		APP													1997:				
										US 1	998-	73852	2 P	P	19980	202			
									1	US 1	997-	99678	33	A1	1997:	1223			
									1	US 1	998-	21898	38	A3	1998	1222			
															1998				

Russel 09/018,879

AB Polyamide oligomers which can be conjugated to lipids, nucleic acids, peptides, proteins, etc., to form liposomes, virusomes, micelles, etc., optionally contg. drugs or biol. agents, have the structure R[NR1(CH2CH2O)m(CH2)pCO(NHCHR2CO)q]nR3 [R = H, alkyl, acyl; each R1 = H, alkyl; or terminal NRR1 = N3; R2 = H, (un)substituted alkyl or aryl, amino acid side chain residue; R3 = H, halogen, OH, SH, alkoxy, NHNH2, NR4R5; R4, R5 = H, alkyl; m = 2-6; n = 4-80; p = 1-4; q = 0, 1]. Thus, tetraethylene glycol was monoetherified with dihydropyran, the resulting acetal etherified with BrCH2CO2Et and deprotected, and the terminal OH replaced by N3 to give N3(CH2CH2O)4CH2CO2Et, part of which was reduced to the NH2 deriv. and part of which was hydrolyzed to the acid, after which the 2 products were condensed by use of dicyclohexylcarbodiimide to give N3(CH2CH2O)4CH2CONH(CH2CH2O)4CH2CO2Et. Two repetitions of this coupling procedure gave N3(CH2CH2O)4CH2CO[NH(CH2CH2O)4CH2CO]7OEt, which was sapond. and converted to N3(CH2CH2O)4CH2CO[NH(CH2CH2O)4CH2CO]7NHCH2CH2OP(O)(OH)OCH2CH[O2C(CH2)16 Me]CH2O2C(CH2)16Me.

IT 154773-34-9P 229645-50-5P, Ethyl 14-amino-3,6,9,12tetraoxatetradecanoate 229645-52-7P 229645-54-9P
229645-56-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(polyamide oligomers for use in drug delivery via liposomes)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15. OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1999:317199 HCAPLUS

DOCUMENT NUMBER: 130:357165

TITLE: Delivery of polyethylene glycol-conjugated molecules

from degradable hydrogels

INVENTOR(S):
Harris, J. Milton

PATENT ASSIGNEE(S): Shearwater Polymers, Inc., USA

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE
WO 9922770	A1 19990514	4 WO 1998-US918 19980123
W: AL, AM,	AT, AT, AU, AZ,	BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
CZ, DE,	DE, DK, DK, EE,	EE, ES, FI, FI, GB, GE, GH, GM, GW, HU,
		KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
		NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SK,	SL, TJ, TM, TR,	TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ,
	KZ, MD, RU, TJ,	
RW: GH, GM,	KE, LS, MW, SD,	SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
FR, GB,	GR, IE, IT, LU,	MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
GA, GN,	ML, MR, NE, SN,	TD, TG
		US 1997-964972 19971105
CA 2304976	AA 19990514	CA 1998-2304976 19980123
AU 9860291	A1 19990524	AU 1998-60291 19980123
AU 752747	B2 20020926	ō
EP 1028753	A1 20000823	B EP 1998-903543 19980123
R: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI		

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JP 2001523637
                       Т2
                             20011127
                                            JP 2000-518700
                                                             19980123
     US 6432397
                       В1
                             20020813
                                            US 1999-426289
                                                             19991025
     US 2002032281
                       A1
                             20020314
                                            US 2001-824265
                                                              20010402
PRIORITY APPLN. INFO.:
                                         US 1997-964972 A 19971105
                                         US 1996-30453P
                                                         P 19961106
                                         WO 1998-US918
                                                          W 19980123
                                         US 1999-426289
                                                          A3 19991025
AΒ
     A degradable, chem. crosslinked PEG hydrogel is described for controlled
     release, by hydrolysis, of conjugates of substantially
     nonpeptidic polymers such as PEG with biol. active mols. For example, PEG
     and protein conjugates can be released in vivo from
     the hydrogels for therapeutic application. The crosslinked hydrogels are
     formed by reaction of (1) active branched derivs. of PEG with (2) amino
     groups on the biol. active mol. and with (3) amino groups on other PEG
     mols. or other nonpeptidic polymers contg. hydrolyzable linkages such as
     carboxylate ester, phosphate ester, acetal, imine, ortho ester,
     peptide, anhydride, ketal, or oligonucleotide linkages in the PEG
     backbone. The hydrolytic breakdown rate can be controlled by variation of
     the hydrolyzable linkage and of the degree of bonding (branching) of the
     branched PEG. Thus, PhCH2(OCH2CH2)nOCH2CO2H was converted to the acid
     chloride with SOC12 and condensed with PhCH2(OCH2CH2)nOH; the resulting
     PhCH2(OCH2CH2)nOCH2CO2(CH2CH2O)nCH2Ph was subjected to hydrogenolysis over
     Pd/C and condensed with disuccinimidyl carbonate to form
     NHS-02C(OCH2CH2)nOCH2CO2(CH2CH2O)nCO2-NHS (NHS = N-hydroxysuccinimidyl).
ΙT
     221630-73-5P 221630-74-6P 224444-84-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (delivery of polyethylene glycol-conjugated mols. from degradable
        hydrogels)
ΙT
     224444-79-5P 224444-89-7P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (delivery of polyethylene glycol-conjugated mols. from degradable
        hydrogels)
REFERENCE COUNT:
                         10
                                THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L15 ANSWER 16 OF 30
                      HCAPLUS COPYRIGHT 2003 ACS
                         1999:242945 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         131:72399
TITLE:
                         Multivalent Thioether-Peptide
                         Conjugates: B Cell Tolerance of an Anti-
                         Peptide Immune Response
                         Jones, David S.; Coutts, Stephen M.; Gamino, Christina A.; Iverson, G. Michael; Linnik, Matthew D.; Randow,
AUTHOR(S):
                         Martina E.; Ton-Nu, Huong-Thu; Victoria, Edward J.
CORPORATE SOURCE:
                         La Jolla Pharmaceutical Company, San Diego, CA, 92121,
                         Bioconjugate Chemistry (1999), 10(3), 480-488
SOURCE:
                         CODEN: BCCHES; ISSN: 1043-1802
                         American Chemical Society
PUBLISHER:
DOCUMENT TYPE:
                         Journal
                         English
LANGUAGE:
     Antibodies which bind .beta.2-glycoprotein I (.beta.2GPI) are assocd. with
     antiphospholipid syndrome. Synthetic peptide mimotopes have
     been discovered which compete with .beta.2GPI for binding to selected
     anti-.beta.2GPI. A thiol-contg. linker was attached to the N-terminus of
     two cyclic thioether peptide mimotopes, peptides la
     and 1b. The resulting peptides, with linker attached, were
     reacted with two different haloacetylated platforms to prep. four
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tetravalent peptide-platform conjugates to be tested as B cell toleragens. The linker-contg. peptides were reacted with maleimide-derivatized keyhole limpet hemocyanin (KLH) to provide peptide-KLH conjugates. Peptides la and lb were also modified by acylation with 3-(4'-hydroxyphenyl)propionic acid N-hydroxysuccinimidyl ester. The resulting hydroxyphenyl peptides were radioiodinated and used to measure anti-peptide antibody levels. The KLH conjugates were used to immunize mice to generate an anti-peptide immune response. The immunized mice were treated with the conjugates or saline soln. and boosted with the appropriate peptide-KLH conjugate. Three of the four conjugates suppressed the formation of antipeptide antibody. The stabilities of the conjugates in mouse serum were measured, and the relative stabilities did not correlate with ability to suppress antibody formation. 186698-35-1P 228403-74-5P

ΙT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of; multivalent thioether-peptide conjugates in relation to B-cell tolerance)

ΙT 134978-94-2

> RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of; multivalent thioether-peptide conjugates in relation to B-cell tolerance)

THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 26 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1998:665874 HCAPLUS

DOCUMENT NUMBER: 130:4084

Preparation of polysaccharide-peptide or TITLE:

amino acid-linked camptothecin conjugates as

antitumor agents

Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Akira; INVENTOR(S):

Yano, Toshiaki

PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent Japanese LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. JP 10273488 A2 19981013 JP 1998-16763 19980129 JP 3322203 В2 20020909

PRIORITY APPLN. INFO.: JP 1997-17280 A 19970131

MARPAT 130:4084 OTHER SOURCE(S):

GI

AB The title compds., which are camptothecin derives. [I; R1 = (un) substituted lower alkyl; X1 = NHR2, OH; wherein R2 = H, lower alkyl; Alk = linear or branched alkylene optionally interrupted by O] linked to carboxy-contg. polysaccharide through a peptide or amino acid, are prepd. These compds. are reduced in toxicity and markedly enhanced in antitumor potency. Claimed is a pharmaceutical compn. contg. I as the active ingredient for treatment of cancers of lung, uterus, ovary, breast, digestive organs (large intestine, stomach, or pancreas), liver, kidney, prostate gland, and neck, malignant lymphoma, and leukemia. Thus, N-peptidyl-10-(3-aminopropoxy)-(20S)-camptothecin deriv. (II; R = H)(prepn. given) was condensed with carboxymethyl dextran sodium salt using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in H2O to give the title compd. II (R = carboxymethyl dextran sodium salt residue), which at 60 mg/kg (single dosage) in vivo inhibited 100% the proliferation of human breast cancer MX-1 cell in mice within 26 days after the drug administration.

IT 215592-09-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of polysaccharide-peptide or amino acid-linked

camptothecin conjugates as antitumor agents)

IT 215592-10-2P 215592-11-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of polysaccharide-peptide or amino acid-linked camptothecin conjugates as antitumor agents)

L15 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1998:603738 HCAPLUS

DOCUMENT NUMBER:

129:302868

TITLE:

Efficient Solid-Phase Synthesis of Peptide-Substituted Alkanethiols for the Preparation of Substrates That

Current the Adhesies of Colle

Support the Adhesion of Cells

AUTHOR(S):

Houseman, Benjamin T.; Mrksich, Milan

CORPORATE SOURCE:

Department of Chemistry, The University of Chicago,

Chicago, IL, 60637, USA

SOURCE: Journal of Organic Chemistry (1998), 63(21), 7552-7555

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE: English The authors describe a rapid and efficient method, based on solid-phase

peptide synthesis, for prepg. alkanethiols terminated with peptide ligands. This methodol. is utilized to synthesize a Gly-Arg-Gly-Asp-Ser alkanethiol conjugate and demonstrate that

monolayers prepd. from this compd. support the adhesion and spreading of fibroblast cells.

214626-69-4P 214626-70-7P 214626-71-8P TТ

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(efficient solid-phase synthesis of peptide-substituted alkanethiols for as cell adhesion substrates)

REFERENCE COUNT:

16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1997:141010 HCAPLUS

DOCUMENT NUMBER:

126:143310

TITLE:

Immunoreactive peptides, conjugates

and methods for treatment of antiphospholipid (aPL)

antibody-mediated pathologies

INVENTOR(S):

Victoria, Edward Jess; Marquis, David Matthew; Jones,

David S.; Yu, Lin

PATENT ASSIGNEE(S):

La Jolla Pharmaceutical Company, USA

SOURCE:

PCT Int. Appl., 118 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	KIND DATE APPLICATION NO. DATE					
WO 9640197	A1	19961219	WO 1996-US9976	19960606			
W: AL, A	AM, AT, AU,	AZ, BB, BG,	BR, BY, CA, CH, CN,	CZ, DE, DK, EE,			
ES, E	FI, GB, GE,	HU, IL, IS,	JP, KE, KG, KP, KR,	KZ, LK, LR, LS,			
LT, I	LU, LV, MD,	MG, MK, MN,	MW, MX, NO, NZ, PL,	PT, RO, RU, SD,			
SE, S	SG .						
RW: KE, I	LS, MW, SD,	SZ, UG, AT,	BE, CH, DE, DK, ES,	FI, FR, GB, GR,			
IE,]	IT, LU, MC,	NL, PT, SE,	BF, BJ, CF, CG, CI,	CM, GA, GN			
US 5874409	A	19990223	US 1995-482651	19950607			
			CA 1996-2223687				
AU 9662710	A1	19961230	AU 1996-62710	19960606			
AU 711192							
EP 833648	A1	19980408	EP 1996-921498	19960606			
			GB, GR, IT, LI, LU,				
IE, E							
CN 1192153	A	19980902	CN 1996-196006	19960606			
JP 11507822	T2	19990713	JP 1996-502123	19960606			
CN 1225015	Α	19990804	CN 1997-196260	19970606			
PRIORITY APPLN. IN	NFO.:	1	JS 1995-482651 A	19950607			
			NO 1996-US9976 W				
OTHER SOURCE(S):	MAR	PAT 126:1433	10				
AB APL analogs t	112111						

09/018,879 Russel Page 20

binds are disclosed. Optimized analogs lacking T cell epitope(s) are useful as conjugates for treating aPL antibody-mediated diseases. Methods of prepg. and identifying said analogs, methods of treatment using said analogs, methods and compns. for prepg. conjugates of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.

134978-94-2 RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of antiphospholipid immunoreactive peptide conjugates for treatment of antiphospholipid antibody-mediated pathologies)

ΙT 118988-07-1P 186698-35-1P 186698-38-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of antiphospholipid immunoreactive peptide conjugates for treatment of antiphospholipid antibody-mediated pathologies)

L15 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1996:184037 HCAPLUS

DOCUMENT NUMBER: 124:254781

TITLE: Conjugates of metal complexes and oligoribonucleotides

which bind specifically to selected target structures

INVENTOR(S): Dinkelborg, Ludger; Hilger, Christoph-Stephan;

Niedballa, Ulrich; Platzek, Johannes; Raduechel,

Bernd; Speck, Ulrich Schering A.-G., Germany PATENT ASSIGNEE(S):

Ger. Offen., 25 pp. SOURCE: CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

Ρ

IT

F	PAT	ENT	NO.		KI		DATE			A	PPLI	CATI	ON N	0.	DATE	2			
I C	JS [L CA	2002 1142 2194	0773 37 558	06	A A A	1 1 1 A	2002 2000 1996	0620 0831 0201		U: I: C:	5 19 L 19 A 19	95-4 95-1 95-2	8829 1423 1945	0 7 58	1995 1995 1995	10714 50607 50620 50630			
			AT, JP,	ΑU,	BB, KR,	BG, LK,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	ES,	FI, RO,	GB,		
		9529	AT, 791	BE,	CH,	DE, 1	1996	0216		Αl	J 19	95-2	9791		1995	NL, 50630 50630		SE	
C H J F Z N	CN HU IP RU ZA NO AU	R: 1152 7632 1050 2165 9505 9700 9920 7213	AT, 879 9 3182 771 895 141 360 30	BE,	CH, A A: T: C: A A: A: B:	DE, 2 2 2 2	DK, 1997 1997 1998 2001 1996 1997 1999 2000	ES, 0625 0828 0324 0427 0219 0314 0617 0629	FR,	GB, CI HI RI RI AI NO AI DE 19	GR, N 19 J 19 P 19 J 19 J 19 J 19 J 19	IE, 95-1 97-1 95-5 97-1 95-5 97-1	IT, 9400 00 0463 0203 895 41 0360 922	LI, 0 0 9 A B2	LU, 1995 1995 1995 1995 1997 1994 1994	MC, 50630 60630 60630 60630 60714 60113 90312 0714 1104	NL,	PT,	SE
									1	DE 19	994-	44450	078	A	1994	1205			

US 1994-357573 B2 19941215 US 1994-358065 B2 19941215 US 1995-409813 B1 19950324 AU 1995-29791 A3 19950630 WO 1995-EP2539 W 19950630

AR Conjugates of modified oligonucleotides with complexes of radioactive or stable metal isotopes, which bind specifically to biol. target structures, are useful in diagnostic imaging and radiotherapy. The oligonucleotides are modified to render them resistant to degrdn. by endogenous nucleases, e.g. by O-alkylation, halogenation, amination, or redn. at the 2' position or by replacement of phosphodiester groups by phosphorothicate, phosphorodithioate, or alkylphosphonate linkages. The oligonucleotides are selected from a random mixt. for binding to a target such as a non-nucleic acid macromol., tissue, or organ. Thus, a 30-mer oligonucleotide ligand for NGF was conjugated with the linker .beta.-cyanoethyl N, N-diisopropylamino-6-(trifluoroacetamido)-1hexylphosphoramidite, then with 10-[7-(4-isothiocyanatophenyl)-2-hydroxy-5oxo-7-(carboxymethyl)-4-azaheptyl]-1,4,7-tris(carboxymethyl)-1,4,7,10tetraazacyclododecane (prepn. given), and complexed with 111In(III) for use as a radiodiagnostic agent.

IT 131274-04-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(conjugates of metal complexes and oligoribonucleotides which bind specifically to selected target structures)

L15 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1995:319762 HCAPLUS

DOCUMENT NUMBER:

122:89553

TITLE:

PEG hydrazone and PEG oxime linkage forming reagents

and protein derivatives.

INVENTOR(S):

Wright, David E.

PATENT ASSIGNEE(S):

Ortho Pharmaceutical Corp., USA

SOURCE:

Eur. Pat. Appl., 47 pp. CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:
FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT NO.	KIND	DATE		APPLICATION NO.	DATE	
	605963	A2 A3	19940713 19951108		EP 1993-309825	19931207	
	•	CH, DE	, DK, ES,	FR, G	B, GR, IE, IT, LI		, PT, SE
	2110543	AA	19940610		CA 1993-2110543		
	9305485	A	19940610		FI 1993-5485	19931208	
NO	9304477	Α	19940610		NO 1993-4477	19931208	
ZA	9309214	A	19950608		ZA 1993-9214	19931208	
AU	9352383	A1	19940623		AU 1993-52383	19931209	
JP	07196925	A2	19950801		JP 1993-340709	19931209	
PRIORITY	APPLN. INFO.	:		US	1992-987739	19921209	
				US	1993-45052	19930407	
				US	1993-157343	19931123	

AB Compds. for modifying polypeptides with PEG or other water-sol. org. polymers are described. The water-sol. polymer reagents include hydrazine, hydrazine carboxylate, semicarbazole, thiosemicarbazide, carbonic acid dihydrazide, carbazide, thiocarbazide, and arylhydrazide derivs. as well as oxylamine derivs. of water-sol. org. polymers, such as polyethylene glycol, polypropylene glycol, polyoxyethylated polyol,

heparin, heparin fragments, dextran polysaccharides, polyamino acids, and polyvinyl alc. Kits for modifying polypeptides with the above water-sol. polymer reagents are also provided. Thus, erythropoietin was modified by oxidn. and treatment with monomethoxypolyoxyethylene semicarbazide and the product was sepd. by chromatog. The antigenicity and the effect on hematocrit levels of the above derivs. were demonstrated.

IT 160556-36-5P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and biol. activity of polyoxyethylene-coupled protein derivs.)

L15 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: DOCUMENT NUMBER:

1994:164909 HCAPLUS

120:164909

TITLE:

Preparation of glycosides and branched sugar

conjugates with peptides or amino

acids as pharmaceutical microparticle carriers Yamada, Harutami; Myoshi, Shiro; Azuma, Kunio; Nakabayashi, Akira; Yamauchi, Hitoshi; Watanabe, Hiroshi; Tanaka, Isao; Sasaki, Atsushi; Murahashi,

Naoichi; Et, Al.

PATENT ASSIGNEE(S):

SOURCE:

INVENTOR(S):

Dei Dei Esu Kenkyusho Kk, Japan Jpn. Kokai Tokkyo Koho, 114 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

LANGUAGE:

Patent Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. PATENT NO. KIND DATE DATE JP 1992-232879 JP 05202085 A2 19930810 19920807 PRIORITY APPLN. INFO.: JP 1991-222214 19910807 GΙ

R1CO (L) NHCO
$$Q=$$

R2O O (CH2) 6NH $Q=$

R1CO (L) NHR $Q=$
NHAc

The title glycopeptides and glycosides (X1 - Xn+1)(AA)n [n = 0,1,2; when n AB = 0, (AA)n = single bond; when n = 1, (AA)n = COCH2CH2(CO-)NH, COCH2(CO-)NH, COCH(CH2O-)NH; when n = 2, (AA)n = COCH2CH2CH(CO-)NH) NHCOCH2CH2CH (CO-) NH, COCH2CH2CH (CO-) NHCOCH (CH2CH2CO-) NH, COCH2CH(CO-)NHCOCH2CH(CO-)NH, COCH2CH(CO-)NHCOCH(CH2CO-)NH, COCH2CH2CH(CO-)NHCOCH(CH2O-)NH, COCH2CH(CO-)NHCOCH(CH2O-)NH, COCH2CH(CO-)NHCOCH(CH2CH2CO-)NH, COCH2CH(CO-)NHCOCH2CH2CH(CO-)NH, COCH2CH2CH(CO-)NHCOCH2CH(CO-)NH; X1 -Xn+1 = OR1 or NHR2 linked to the CO group of (AA)n, R linked to the oxy

group of (AA)n; wherein R = (acetyl-protected) glycosyl group; R1 = H, alkali metal, C1-3 alkyl, CH2Ph; R2 = H, (CH2)aOR, (CH2CH2O)bR; a = 1-10; b = 1-8; some provisos given], useful as materials for liposomes for selectively delivering pharmaceuticals to organs, e.g. liver, and with improved microcirculation, are prepd. Thus, N-deprotection of galactosamine-contg. diglutamic acid deriv. (I; R = Me3CO2C, R1 = Q, R2 = Ac) (prepn. given) with CF3CO2H followed by amidation with HO2CCH2(OCH2CH2)3OC18H37 using DCC and N-hydroxysuccinimide in CH2C12 contg. Et3N gave I [R = C18H37(OCH2CH2)3OCH2CO, R1 = Q, R2 = Ac] which was O-deacetylated with NaOMe in MeOH to give I [R = C18H37(OCH2CH2)3OCH2CO, R1 = Q, R2 = H]. Liposomes contg. 3H-inulin were prepd. from L-palmitoylphosphtidylcholin, choresterol, dicetyl phosphate, and H3-inulin and administered to rats i.v. The liposomes rapidly disappeared from blood and were transfered to liver.

IT 153253-81-7

RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, in prepn. of organ-selective liposome material)

L15 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:560829 HCAPLUS

DOCUMENT NUMBER: 119:160829

TITLE: One vial method for labeling protein/linker

conjugates with technetium-99m

INVENTOR(S): Dean, Richard T. PATENT ASSIGNEE(S): Centocor, USA SOURCE: U.S., 20 pp.

OURCE: U.S., 20 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
US 5180816	A	19930119		US 1988-235908	19880824
PRIORITY APPLN. IN	·O.:		US	1988-235908	19880824
OTHER SOURCE(S):	MA	RPAT 119:160	829		
GI					

AB A one-vial method for labeling proteins with radioisotopes
Tc-99m, Re-186, Re-188, Re-189 and Re-191 is disclosed. The method
comprises contacting in a single vial a mixt. of a reducing agent and a
protein mol. covalently bound to sulfhydryl contg. bifunctional
coupling agents RS(CH2)aCO(NHCHR3CO)f(OCH2CH2)cZ,
RS(CH2)aCO(NHCHR3CO)f(OCH2CH2)cOCH2CO(OCH2CH2)cZ, or

Ι

RS(CH2)aCO(NHCHR3CO) fOCH2CONHCH2CH2Z [a = 1-3; c = 1-7; f = 3-6; R = R1CO or R1S [R1 = (un)substituted alkyl or aryl]; R3 = H, (un)substituted alkyl or aryl; Z = C1CH2CONH, BrCH2CONH, ICH2CONH, N-substituted maleimido] with radioactive Tc or Re in an oxidized state. Thus, peptide deriv. I was prepd. and then coupled to antimyosin Fab'. The above conjugate was labeled with technetium-99m by treatment with sodium [Tc-99m]pertechnetate from a Mo-99/Tc-99m generator in the presence of glucarate and stannous ions.

IT 146551-11-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)

L15 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:534568 HCAPLUS

DOCUMENT NUMBER: 119:134568

TITLE: Crosslinking protein compositions having two or more

identical binding sites for targeting therapy or

diagnosis

INVENTOR(S): Dean, Richard T.; Lister-James, John; Boutin, Raymond

Н.

PATENT ASSIGNEE(S): Centocor, Inc., USA

SOURCE: U.S., 10 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5185433	A	19930209	US 1990-506122	19900409
PRIORITY APPLN.	INFO.:		US·1990-506122	19900409
GI				

AB The present invention provides crosslinked protein compns. consisting of .gtoreq.2 units of a target-specific protein (antibody) joined by binding SH groups on the target-specific protein units to a SH-selective crosslinking agent. These crosslinked protein compns. combine an increase in binding

affinity due to the presence of multiple identical binding sites and stability to reducing conditions. Therapeutic moieties or radiotracers may be attached to the crosslinked target-specific protein compn. for targeting therapy or radiodiagnosis. Thus, 99mTc-labeled crosslinked antiovarian cancer OC125 F(ab')2-I conjugate for radiodiagnosis was prepd. by (1) treating OC 125 F(ab')2 with II and iodoacetamide and (2) treating the crosslinked OC 125 F(ab')2 with I and then 99mTc glucarate.

ΙT 131274-04-9DP, conjugates with antibodies and other substances 149299-81-ODP, conjugates with antibodies and other substances

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, for targeting diagnosis or therapy)

L15 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1993:503320 HCAPLUS

DOCUMENT NUMBER: 119:103320

TITLE: Proteins conjugates with

positively charged molecules with decreased blood

clearance rates

INVENTOR(S): Dean, Richard T.; Boutin, Raymond H.; Lister-James,

John

PATENT ASSIGNEE(S): Centocor, USA SOURCE: U.S., 11 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 5162505 A 19921110 US 1989-409150 19890919 US 1989-409150 19890919 ----PRIORITY APPLN. INFO.:. US
OTHER SOURCE(S): MARPAT 119:103320

Protein conjugates comprising a protein covalently linked to .gtoreq.1 pos. charged mol., so that it has an overall net pos. charge in aq. conditions at physiol. pH, are disclosed. The pos. charged mol. comprise polymers of .gtoreq.3 subunits selected from the group consisting of amino acids contg. pos. charged side chains and alkylamines. The protein conjugates have decreased blood clearance rates compared to conjugates which do not have the pos. charged mol. The protein conjugates may further comprise diagnostic or therapeutic radionuclides bound to the protein or pos. charged mol. through bifunctional coupling agents. Penta-L-lysine-antimyosin Fab' conjugate (prepn. is given) was added to a soln. of succinimidyl benzothioacetylglycylglycinate and the modified protein conjugate was purified by Sephadex chromatog. The purified protein conjugate was deprotected and labeled with 99Tc. The deprotected and labeled protein conjugate was applied to a myosin-Sepharose column and bound and unbound fractions were counted and immunoreactivity detd. The immunoreactivity and recovery was 97, and 93% resp. The biodistribution of the protein conjugate was studied in mice.

ΙT 149299-81-0P

RL: PRP (Properties); PREP (Preparation) (prepn. and conjugation of, with proteins)

L15 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1993:148067 HCAPLUS

DOCUMENT NUMBER: 118:148067

TITLE: Preparation of bifunctional coupling agents as

scintigraphic agents

INVENTOR(S): Dean, Richard T.; Boutin, Raymond H.; Weber, Robert W.

PATENT ASSIGNEE(S): Centocor, USA

SOURCE: U.S., 17 pp. Cont.-in-part of U.S. Ser. No. 207,261.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	API	PLICATION NO	. DATE
US 5144043	A	19920901	US	1988-235999	19880824
US 5218128	A	19930608	US	1988-207261	19880615
PRIORITY APPLN. IN	FO.:		US 198	38-207261	19880615
OTHER SOURCE(S):	MA	RPAT 118:148	3067		
AB The title cou	pling age	nts were pre	epd. for	joining sul	lfhydryl-co
			• •		

The title coupling agents were prepd. for joining sulfhydryl-contg.

proteins or peptides and metallic radionuclides. These
agents contain a sulfhydryl-selective electrophile, a chelator contg.

gtoreq.l protected thiol, and a linker. The title compds. are useful as immunodiagnostic and radiotherapeutic agents. Thus,

PhCOSCH2CO(NHCH2CO)2NHCH2CO2H was esterified by Boc-NHCH2CH2OCH2CH2OH and the product was deprotected by CF3CO2H and then N-alkylated with BrCOCH2Br to give the PhCOSCH2CO(NHCH2CO)3O(CH2)O(CH2)2NHCOCH2Br (I) in 6% yield. I was conjugated with antifibrin antibody Fab' fragments, labeled

with 99mTc, and the biodistribution of the labeled conjugate was detd.

IT 131274-04-9DP, antifibrin Fab' and Tc-99m conjugates 146551-07-7DP, antifibrin Fab' and Tc-99m conjugates 146551-09-9DP, antifibrin Fab' and Tc-99m conjugates 146551-11-3DP, antifibrin Fab', antimyosin Fab' and Tc-99m

conjugates
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and biodistribution of)
IT 131274-04-9P 146551-07-7P 146551-09-9P

131274-04-9P 146551-07-7P 146551-09-9
146551-11-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as bifunctional coupling agent for metallic radionuclide and sulfhydryl-contg. protein or peptides)

IT 146551-24-8P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as intermediate for bifunctional coupling agents)

L15 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1992:152389 HCAPLUS

DOCUMENT NUMBER: 116:152389

TITLE: Preparation of improved marked haptens for immunoassay

INVENTOR(S): Kinkel, Tonio; Mayer, Andreas; Neuenhofer, Stephan;

Oekonomopulos, Raymond

PATENT ASSIGNEE(S): Hoechst A.-G., Germany SOURCE: Ger. Offen., 22 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATEN	IT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 40	04296	A1	19910814	DE 1990-4004296	19900213
EP 44	2372	A1	19910821	EP 1991-101656	19910207
EP 44	2372	B1	19950503		
R	: AT, BE,	CH, DE,	DK, ES,	FR, GB, IT, LI, NL	
AT 12	2149	E	19950515	AT 1991-101656	19910207
ES 20	74179	Т3	19950901	ES 1991-101656	19910207
PRIORITY A	PPLN. INFO.	. :		DE 1990-4004296	19900213
GT	•				

HO
$$\longrightarrow$$
 O \longrightarrow O \longrightarrow CO₂H O (OCH₂CH₂)_bNH $_3^{\dagger}$ CF₃CO $_2^{-}$

AB (XY) nZQm [X = biol. active substance (hapten); Y = COA(OCH2CH2)xNH, etc.; A = alkylene, CH2NHCO; x = 1-60; Z = protein, polypeptide; Q = chem. or phys. quantifiable labeling group; m, n = 1-4], useful in (chemiluminescent) immunoassay of haptens in liqs. (no details), were prepd. Thus, polyethylene glycol 600 was monochlorinated with SOC12 in pyridine and the product was treated with N2CHCO2Et/BF3-Et2O, and then with NaN3 in DMF to give the monoazidomonocarboxylic acid deriv. This was hydrogenated in EtOH/CH2Cl2 over Pd/C followed by N-protection with triiodothyronine, and deprotection to give intermediate I (b .apprxeq. 7-19). This may be treated successively with poly(Glu:Lys 6:4)/ .gamma. maleimidobutyric acid N-succinimidyl ester, S-acetylmercaptosuccinic anhydride, hydroxylamine hydrochloride, mercaptopropionic acid, and N-(4-methoxyphenyl)-N-[4-(2-succinimidyloxycarbonylethyl)benzenesulfonyl]-10-methylacridinium-9-carboxamide fluorosulfonate to give a title compd. IΤ 139729-26-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as intermediate for improved marked hapten)

L15 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1992:106333 HCAPLUS

DOCUMENT NUMBER:

116:106333

TITLE:

Preparation of tetraazacycloalkane chelating agents

Ι

and conjugates with proteins

INVENTOR(S):

Dean, Richard T.; Weber, Robert W.

PATENT ASSIGNEE(S): SOURCE:

Centocor, Inc., USA

booker.

U.S., 11 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5053503	Α	19911001	US 1989-312767	19890217

PRIORITY APPLN. INFO.: US 1989-312767 19890217

OTHER SOURCE(S): MARPAT 116:106333

GΙ

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and II; (E = group capable of reacting with a site on a protein; L = org. linking radical which may contain a cleavable site; R, R1 = H, alkyl; m, n, p, q = 2, 3; v, w = 0-2), and conjugates thereof, were prepd. Thus, 1,4,7,10-tetraazacyclododecane was converted to tetraalkylated title compd. III in several steps. III was stirred with antimyosin Fab' in DMF and the resulting conjugate was treated with 111InCl3 to give the radioactively labeled conjugate.

IT 139085-82-8DP, reaction products with proteins and metal

Saits

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as drugs and diagnostics)

IT 139085-86-2P

CORPORATE SOURCE:

SOURCE:

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as intermediate for chelating agents-protein conjugates)

L15 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1991:38509 HCAPLUS

DOCUMENT NUMBER: , 114:38509

TITLE: Enhanced kidney clearance with an ester-linked

99mTc-radiolabeled antibody Fab'-chelator conjugate

AUTHOR(S): Weber, Robert W.; Boutin, Raymond H.; Nedelman, Mark

A.; Lister-James, John; Dean, Richard T. Centocor, Inc., Malvern, PA, 19355, USA Bioconjugate Chemistry (1990), 1(6), 431-7

CODEN: BCCHES; ISSN: 1043-1802

DOCUMENT TYPE: Journal LANGUAGE: English

AB Bifunctional chelators for labeling antibodies with 99mTc, based on the N3S core of mercaptoacetyltriglycine having ester or amide linking moieties, were synthesized and site-specifically attached to the sulfhydryl groups of the Fab' fragment of antimyosin. Protein labeling was quant. after 15 min; postlabeling purifn. was not necessary. The radiolabeled conjugates exhibited no loss of immunoreactivity. Under basic conditions, the ester-linked conjugate lost 95% of the radiolabel in the form of the 99mTc complex of mercaptoacetyltriglycine as detd. by reversed-phase HPLC, whereas the radioactivity in the amide-linked conjugate remained completely bound to the protein. In a mouse biodistribution study, the ester-linked conjugate showed a 2-fold enhancement in clearance from the kidney when compared to the amide-linked product.

IT 131274-04-9P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and conjugation of, with technetium-99m and antibody
 F(ab')2 fragment)

L15 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1982:97667 HCAPLUS

DOCUMENT NUMBER: 96:97667

TITLE:

Phencyclidine conjugates to antigenic

proteins and enzymes

INVENTOR(S):

Lin, Cheng I.; Singh, Prithipal

PATENT ASSIGNEE(S): SOURCE:

Syva Co., USA U.S., 6 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

Ι

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE ----------_____ US 1979-6935 US 4281065 A 19810728 19790125 PRIORITY APPLN. INFO.: US 1979-6935 19790125 GΙ

AB Phencyclidine deriv. conjugates with antigenic proteins and enzymes I [X and X1 = alkylene, R = poly(amino acid)] are synthesized and employed for the prodn. of antibodies for use in immunoassays and enzyme immunoassays of phencyclidene, resp. Thus, 5-(4-(1piperidinocyclohexan-1-yl)phenyl)-3-oxapentanoic acid [79849-45-9] was synthesized and conjugated with glucose 6-phosphate dehydrogenase [3867-15-0]. The resulting conjugate was sensitive to small changes in phencyclidine concns.

ΙT 79849-47-1P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and hydrolysis of)

=> select hit rn 115 1-30 ENTER ANSWER SET OR SMARTSELECT L# OR (L15):end

=> select hit rn 115 1-30 E1 THROUGH E77 ASSIGNED

=> fil req

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 APR 2003 HIGHEST RN 502545-60-0 DICTIONARY FILE UPDATES: 9 APR 2003 HIGHEST RN 502545-60-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> fil hcaplu FILE 'HCAPLUS' ENTERED AT 15:42:55 ON 10 APR 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 10 Apr 2003 VOL 138 ISS 15 FILE LAST UPDATED: 9 Apr 2003 (20030409/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d stat que
L1 STR

9
O
CH2·C~O-~ CH2·CH2·O~ CH2·CH2

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L2 (6984)SEA FILE=REGISTRY SSS FUL L1
L3 (10066)SEA FILE=HCAPLUS L2

Page 31 '

INVENTOR(S):

conjugates and methods of synthesizing same

Soltero, Richard; Radhakrishnan, Balasingham;

```
Ekwuribe, Nnochiri N.
PATENT ASSIGNEE(S):
                         Nobex Corporation, USA
SOURCE:
                         PCT Int. Appl., 113 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                     KIND DATE
                                           APPLICATION NO. DATE
                           -----
                                           -----
                            20030320
     WO 2003022996
                     A2
                                          WO 2002-US28428 20020906
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                        US 2001-318197P P 20010907
                                        US 2001-36744
                                                         A 20011221
                                        US 2002-349462P P 20020118
     Methods for synthesizing proinsulin polypeptides are described
AB
     that include a contacting a proinsulin polypeptide including an
     insulin polypeptide coupled to one or more
     peptides by peptide bond(s) capable of being cleaved to
     yield the insulin polypeptide with an oligomer under
     conditions sufficient to couple the oligomer to the insulin
    polypeptide portion of the proinsulin polypeptide and
     provide a proinsulin polypeptide-oligomer conjugate,
     and cleaving the one or more peptides from the proinsulin
    polypeptide-oligomer conjugate to provide the
     insulin polypeptide-oligomer conjugate.
    Methods of synthesizing proinsulin polypeptide-oligomer
     conjugates are also described as are proinsulin
    polypeptide-oligomer conjugates. Methods of
     synthesizing C-peptide polypeptide-oligomer
     conjugates are also described.
IT
     9004-10-8DP, Insulin, conjugates
     9035-68-1DP, Proinsulin, conjugates
     RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (synthesizing insulin polypeptide-oligomer
       conjugates and proinsulin polypeptide-oligomer
       conjugates)
IT
    477775-76-1P 502487-24-3P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (synthesizing insulin polypeptide-oligomer
       conjugates and proinsulin polypeptide-oligomer
       conjugates)
ΙT
    59112-80-0D, c peptide, conjugates
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (synthesizing insulin polypeptide-oligomer
```

conjugates and proinsulin polypeptide-oligomer

conjugates) L21 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2003:221462 HCAPLUS TITLE: Pharmaceutical compositions of drug-oligomer conjugates for oral administration INVENTOR(S): Soltero, Richard; Ekwuribe, Nnochiri N.; Opawale, Foyeke; Rehlaender, Bruce; Hickey, Anthony; Bovet, Li Li PATENT ASSIGNEE(S): Nobex Corporation, USA SOURCE: PCT Int. Appl., 96 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE WO 2003022210 A2 20030320 WO 2002-US28536 20020906 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.:

US 2001-318193P P 20010907 US 2002-377865P P 20020503

An oral pharmaceutical compn. comprising a drug-oligomer conjugate AB , 0.1-15% of a fatty acid component, and 0.1-15% of a bile salt component is described. The drug, e.g., a peptide or protein, is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component are present in a wt.-to-wt. ratio of between 1:5 and 5:1. Methods of treating diseases in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. For example, tablets contg. an insulin conjugate HIM2 were prepd. by lyophilization of a mixt. contg. HIM2 2.5 g, Na cholate 30.0 g, oleic acid 10.0 g, 25% sucralose 8.0 g, flavor 4.0 g, capric acid 5.0 g, lauric acid 5.0 g, citric acid 67.2 g, trolamine 42.4 g, NaOH 18.8 g, pH adjusters (5N NaOH and 5N HCl) as needed, and water resulting in an amorphous powder. The powder (127.6 g) was blended with citric acid 29.7 g, sodium citrate 84.2 g, Tris base 106.7 g, microcryst. cellulose 24.8 g, and Explotab 9.4 g and compressed into tablets.

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

- ΙT 11061-68-0D, Human insulin, conjugates with methoxy(polyethylene glycol) hexanoic acid RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oral compns. of drug-oligomer conjugates contg. bile salt and fatty acid)
- ΙT 59112-80-0D, C-Peptide, oligomer conjugates RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

```
(oral compns. of drug-oligomer conjugates contg. bile salt
        and fatty acid)
ΙT
     10108-28-8P 113395-48-5P 477775-74-9P
     477775-75-0P 477775-76-1P 502487-23-2P
     502487-24-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (prepn. of oligomers for drug-oligomer conjugates for oral delivery)
L21 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
                          2003:221460 HCAPLUS
TITLE:
                          Pharmaceutical compositions of insulin
                          drug-oligomer conjugates
INVENTOR(S):
                           Soltero, Richard; Radhakrishnan, Balasingham;
                          Ekwuribe, Nnochiri N.; Rehlaender, Bruce; Hickey,
                          Anthony; Bovet, Li Li
                          Nobex Corporation, USA
PATENT ASSIGNEE(S):
SOURCE:
                          PCT Int. Appl., 65 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                     KIND DATE
                                     APPLICATION NO. DATE
                                             ______
                             _____
                                        WO 2002-US28429 20020906
     WO 2003022208 A2 20030320
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RQ, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
              RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
              CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                          US 2001-318193P P 20010907
                                          US 2002-377865P P 20020503
     Pharmaceutical compns. that include an insulin drug-oligomer
AB
     conjugate, a fatty acid component, and a bile salt component are
     described. The insulin drug is covalently coupled to an
     oligomeric moiety. The fatty acid component and the bile salt component
     are present in a wt.-to-wt. ratio of between 1:5 and 5:1. Methods of
     treating an insulin deficiency in a subject in need of such
     treatment using such pharmaceutical compns. are also provided, as are
     methods of providing such pharmaceutical compns. E.g., PEG derivs. of
     fatty acids such as hexanoic acid were prepd., activated and
     conjugated to insulin derivs.
     10108-28-8P 113395-48-5P 259228-98-3P
IT
     477775-74-9P 477775-75-0P 477775-76-1P
     502487-23-2P 502487-24-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (pharmaceutical compns. of insulin drug-oligomer
        conjugates)
ΙT
     9004-10-8DP, Insulin, conjugates with fatty
     acid-PEG derivs.
```

L21 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2003:114145 HCAPLUS

DOCUMENT NUMBER: 138:149948

TITLE: Cell having modified cell membrane

INVENTOR(S): Nagamune, Teruyuki; Itoh, Chika; Yasukohchi, Tohru;

Ohhashi, Syunsuke; Kubo, Kazuhiro

PATENT ASSIGNEE(S): NOF Corporation, Japan SOURCE: Eur. Pat. Appl., 21 pp. CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

EP 1283257 A2 20030212 EP 2002-17552 20020807

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK PRIORITY APPLN. INFO.:

JP 2001-241843 A 20010809

AB A cell in which a reaction product of a substance to be modified and an amphipathic compd. is non-covalently bound to a cell membrane, wherein said compd. has the following features: (1) having one or more aliph. hydrocarbon groups at one end; (2) having one or more portions contg. a hydrophilic group in a mol.; and (3) having one or more reactive functional groups which are capable of covalently binding with the substance to be modified at an end different from the end in the above (1). Fluorescein-polyethylene oxide-modified

dioleoylphosphatidylethanolamine was prepd. and stably anchored in mouse fibroblast NIH3T3 cell membranes.

IT 496050-85-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cell having cell membrane modified by noncovalently bound reaction product of substance and amphipathic compd.)

IT 496050-86-3DP, fluorescein derivs.

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(noncovalent binding to cell membrane; cell having cell membrane modified by noncovalently bound reaction product of substance and amphipathic compd.)

L21 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2000:757702 HCAPLUS

DOCUMENT NUMBER: 134:71479

TITLE: Synthesis and antiproliferative activity of

. unsaturated quinoline derivatives

AUTHOR(S): Montgomery, Gerard J.; McKeown, Paul; McGown, Alan T.;

Robins, David J.

CORPORATE SOURCE: Department of Chemistry, University of Glasgow,

Glasgow, G12 8QQ, UK

SOURCE: Anti-Cancer Drug Design (2000), 15(3), 171-181

CODEN: ACDDEA; ISSN: 0266-9536

PUBLISHER: Oxford University Press

Russel 09/018,879 Page 36

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 134:71479

Knoevenagel condensation of quinoline 6-, 7- and 8-carboxaldehyde with malononitrile derivs. was used to produce a series of 23 quinoline-tyrphostins. Some of these heteroarom. tyrphostins were potent inhibitors of the epidermal growth factor (EGF) receptor kinase and were moderately active against the MCF7 breast cancer cell line. The order of potency was 7- > 6- > 8-substituted quinoline, which indicates that increased activity of the 7-substituted quinolines is assocd. with electron deficiency at the 7-position in the quinoline ring. The most active compd., formed from 7-quinolinecarboxaldehyde and Et cyanoacetate, had an IC50 value of 2.3 .mu.M. The prepd. compds. showed similar IC50 values against the MCF7 and MCF7/ADR cell lines (the latter shows fourfold increased protein tyrosine kinase activity) except for the compds. formed from 6-quinolinecarboxaldehyde and malononitrile and 7-quinolinecarboxaldehyde and cyanoacetamide, which showed a significant (11- and 42-fold, resp.) increase in potency against the MCF7/ADR cell line. Furthermore, no assocn. was found between growth inhibition and inhibition of the EGFR protein tyrosine kinase (PTK), using a cell-free assay. In addn., new compds. were prepd. from 2- and 4-quinolinecarboxaldehyde with extended conjugation in the side chains or with methoxypolyethoxyethyl esters in the side chain to increase water soly. These compds. showed substantial cytotoxicity, with IC50 values in the range 1-25 .mu.M, but similar values were obsd. against both cell lines. No assocn. was found between inhibition of PTK and growth inhibition, again indicating that their mode of action may not be specific for the EGF receptor.

ΙT 315178-31-5P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and Knoevenagel condensation with quinolinecarboxaldehydes) , 20 REFERENCE COUNT: THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS 1998:471436 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 129:78811

TITLE: Receptor membranes.

INVENTOR(S): Cornell, Bruce Andrew; Braach-maksvytis, Vijolrta

Lucija Brinislava

PATENT ASSIGNEE(S): Australian Membrane and Biotechnology Research

Institute, Australia

U.S., 14 pp. CODEN: USXXAM SOURCE:

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5766960	Α	19980616	US 1995-449895	19950523
US 5436170	\cdot A	19950725	US 1990-473932	19900125
US 5693477	А	19971202	US 1995-447569	19950523
US 5741712	A	19980421	US 1995-448178	19950523
PRIORITY APPLN. II	NFO.:		AU 1987-3346	19870727
			AU 1987-3348	19870727
			AU 1987-3453	19870731

```
AU 1987-4478 19870921
US 1990-473932 19900125
WO 1988-AU273 19880727
AB A membrane comprising a closely packed array of self-assembling amphiphilic mols., and is characterized in that it incorporates a plurality of ion channels, and/or at least a proportion of the
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plurality of ion channels, and/or at least a proportion of the self-assembling mols. comprise a receptor mol. conjugated with a supporting entity. The ion channel is selected from the group consisting of peptides capable of forming helixes and aggregates thereof, coronands, cryptands, podands and combinations thereof. In the amphiphilic mols. comprising a receptor mol. conjugated with a supporting entity, the receptor mol. has a receptor site and is selected from the group consisting of Igs, antibodies, antibody fragments, dyes, enzymes and lectins. "The supporting entity is selected from the group consisting of a lipid head group, a hydrocarbon chain(s), a cross-linkable mol. and a membrane protein. The supporting entity is attached to the receptor mol. at tan end remote from the receptor site. In preferred embodiments the ion channel is gramicidin A, and is preferable gated. Such membranes may be used in the formation of sensing devices.

IT 124804-88-2P 124804-89-3P 209266-70-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(receptor membranes)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1996:761698 HCAPLUS

DOCUMENT NUMBER: 126:33023

TITLE: Hybrid phthalocyanine derivatives and their uses INVENTOR(S): Buechler, Kenneth F.; Noar, Joseph B.; Tadesse, Lema

PATENT ASSIGNEE(S): Biosite Diagnostics Incorporated, USA

SOURCE: PCT Int. Appl., 190 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

P	ATENT	NO.		KI	ND :	DATE			A	PPLI	CATI	ои ис	ο.	DATE			
M(9629	367		A:	1	1996	0926		W	0 19	 96-U	 s383:	- <i>-</i> 3	1996	0322		
•	W:	•		•				•	-	-		-	-	CZ, LK,			
•		•	LV,	•	•	•	•	•	•	•			•	RO,	•	•	•
	RW:	KE,	LS,											FI, CM,			
	A 2215	727		A	A	1996	0926		C.	A 19	96-2	2157	27	1996	0322	GIV,	1117
	U 9653 P 8204																
E	P 8204	89 AT,						ΤT.	T.T.	NT.							
	P 1050	8897	·	T	2	19980	902		J	P 19				19960			
PRIORI:	r 2030 ry Apr				•	20010)/15	I	US 1	995-	40982	25	Α	19950	323		
		, ,												19960			

AB Water-sol. hybrid phthalocyanine derivs., fluorescent latex particles incorporating which are useful in competitive and noncompetitive immunoassays and nucleic acid assays, have (1) .gtoreq.l donor subunit

with a desired excitation peak and (2) .gtoreq.1 acceptor subunit with a desired emission peak, and are capable of intramol. energy transfer from the donor subunit to the acceptor subunit. They may also contain an electron-transfer subunit. Axial ligands may be covalently bound to the metals contained in the water-sol. hybrid phthalocyanine derivs. Ligands, ligand analogs, polypeptides, proteins, and nucleic acids can be linked to the axial ligands of the dyes to form conjugates useful in immunoassays and nucleic acid assays.

183872-90-4P 183873-00-9P

RL: IMF (Industrial manufacture); PREP (Preparation) (prepn. of water-sol. fluorescent hybrid phthalocyanine derivs. for immunoassays)

L21 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1996:630259 HCAPLUS

DOCUMENT NUMBER: 125:269871

TITLE: Polymer compositions and methods for directed

ultrasound imaging

INVENTOR(S): Quay, Steven C.; Marrs, Christopher M.; Worah, Dilip

Μ.

PATENT ASSIGNEE(S): Sonus Pharmaceuticals, Inc., USA

SOURCE: Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

ΙT

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 727225	A2	19960821	EP 1996-630007	19960208
EP 727225	·A3	19970115		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE JP 08325165 A2 19961210 JP 1996-52387 19960214 PRIORITY APPLN. INFO.: US 1995-388468 19950606

AB Compns. for enhancing the ability to target gaseous microbubbles used in ultrasound contrast are described. The compns. include a cell adhesion mol. ligand which is incorporated into a desired mol. to form a conjugate. When the contrast agent is a colloidal dispersion, the conjugate is formed with a surfactant. When the agent is a solid microsphere, the conjugate is formed with a portion of the solid. Once the conjugate is formed, the surfactant or microsphere will adhere to the surface of desired target cells by coupling of the CAM ligand to cell adhesion mols. expressed on the cell surface. Thus, Jeffamine M-2070 was allowed to react with Sialyl Lewis X in the presence of NaCNBH3 and the product formed was uses in compns. and.

IT 182232-90-2P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (polymer compns. for directed ultrasound imaging)

L21 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1994:573281 HCAPLUS

DOCUMENT NUMBER: 121:173281

TITLE: Caged Protein Conjugates and

Light-Directed Generation of Protein

Activity: Preparation, Photoactivation, and Spectroscopic Characterization of Caged G-Actin Conjugates

AUTHOR(S):

Marriott, Gerard

CORPORATE SOURCE:

Biomolecular and Cellular Dynamics Research Group, Max

Planck Institute for Biochemistry, Martinsried bei

Muenchen, 82152, Germany

SOURCE:

Biochemistry (1994), 33(31), 9092-7

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE:

Journal

LANGUAGE: English

A simple method is described to prep. caged (inactive) protein complexes using the amino group-directed photo-deprotection group [(nitroveratryl)oxy]chlorocarbamate (NVOC-Cl). This report describes how the polymn. activity of G-actin in physiol. salt soln. is lost upon conjugation of essential lysine residues of G-actin with NVOC-Cl. Reaction conditions were optimized to prep. caged G-actin in high yield, and the conjugate was characterized by biochem. and absorption spectroscopic methods. Upon excitation of caged G-actin in physiol. salt solns. with near-UV light, an efficient photo-deprotection reaction occurs via photoisomerization of the (nitrophenyl)ethylgroup of NVOC, which results in cleavage of the carbamate linkage between the protection reagent and G-actin. A std. irradn. condition was then defined which leads to photoactivation of F-actin from caged G-actin with a yield of more than 90%. Photoactivated F-actin was characterized according to its sedimentation behavior, electron microscopic anal., and sliding velocity on heavy meromyosin detd. with the in vitro motility assay. The results of these assays were similar to those obtained from unmodified F-actin. I also report the prepn. of caged G-actin conjugated at cysteine 374 with tetramethylrhodamine iodoacetamide and caged fluorescein These caged G-actin conjugates can be used to maleimide. generate fluorescent, polymn. competent G-actin following near-UV irradn. Given the widespread applications of caged substrates and ligands in cell biol., the simple method described herein to prep. and photoactivate caged protein conjugates is expected to advance investigations on the regulation of protein activity in living cells.

IT 250580-74-6P

> RL: SPN (Synthetic preparation); PREP (Preparation) (controlled drug release from, polymer blends in relation to)

L21 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS

1994:477743 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

121:77743

TITLE:

Sensor membranes containing ionophores for ion selective electrodes and biosensors and their preparation and use in the detection of analytes

INVENTOR(S):

Raguse, Burkhard; Cornell, Bruce Andrew;

Braach-Maksvytis, Vijoleta Lucija Bronislava; Pace,

Ronald John

PATENT ASSIGNEE(S):

Australian Membrane and Biotechnology Research

Institute, Australia; University of Sydney

SOURCE:

PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407593	A1	19940414	WO 1993-AU509	19931001

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AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP,
            KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU,
            SD, SE, SK, UA, US, VN
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
            BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
                                           EP 1993-922449
    EP 670751
                       A1
                            19950913
                                                             19931001
    EP 670751
                       В1
                            20011212
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
                                            JP 1993-508531
                                                             19931001
    JP 08505123
                       T2
                            19960604
                                            AU 1993-51444
                                                             19931001
    AU 672638
                       B2
                            19961010
    AU 9351444
                       Α1
                            19940426
                                            EP 2001-105279
                                                             19931001
    EP 1104883
                       A2
                            20010606
    EP 1104883
                       А3
                            20010718
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
                                                             19931001
    EP 1106998
                       Α2
                            20010613
                                            EP 2001-105278
    EP 1106998
                       A3
                            20010718
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
                                                            19931001
                                            EP 2001-105275
                            20010905
    EP 1130386
                       Al
                BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
            AT,
                                            EP 2001-105276
                                                             19931001
                            20010905
   · EP 1130387
                       Α1
                 BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
            AT,
                                                             19931001
                                            EP 2001-105277
    EP 1130388
                       Α1
                            20010905
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
                                            AT 1993-922449
                                                             19931001
    AT 210731
                       Ε
                            20011215
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                                                             19931001
    ES 2169725
                       Т3
                            20020716
                            19970610
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                                                             19950517
    US 5637201
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                                                             19970409
    US 5741409
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                            19980421
                                            US 1997-833786
                                            US 1997-833782
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    US 5753093
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                            19980519
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                            19980721
                                            US 1997-826904
                                                             19970409
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                       Α
                                                          A 19921001
                                        AU 1992-5069
PRIORITY APPLN. INFO.:
                                                          A 19930708
                                        AU 1993-9863
                                                          A3 19931001
                                         EP 1993-922449
                                                          W
                                                             19931001
                                         WO 1993-AU509
                                                          A3 19950517
                                         US 1995-406853
```

The present invention relates to electrode membrane combinations for use AΒ in ion selective electrodes and biosensors. In addn., the present invention relates to methods for the prodn. of such electrode membrane combinations and the use of ion selective electrodes and biosensors incorporating such electrode membrane combinations in the detection of analytes. The present invention also relates to novel compds. used in the electrode membrane combinations. These novel compds. include a linker lipid for use in attaching a membrane including a plurality of ionophores to an electrode and providing a space between the membrane, the electrode being either in part or totally made up of the linker lipid. The linker lipid comprises within the same mol. a hydrophobic region capable of spanning the membrane, an attachment group used to attach the mol. to an electrode surface, a hydrophilic region between the hydrophobic region and the attachment group, and a polar head group region attached to the hydrophobic region at a site remote from the hydrophilic region. A Au on glass electrode was immersed in a soln. of 23-(20'-oxo-19'-oxaeicosa-(Z)-9'-ene)-70-phenyl-20,25,28,42,45-pentaoxo-24-aza-19, 29, 32, 35, 38, 41, 46, 47, 52, 55-decaoxa-58, 59-dithioahexaconta-(Z)-9-ene linker lipid and bis(2-hydroxyethyl)disulfide, the disulfide was allowed to adsorb, and the electrode was rinsed, dried, and clamped in a containment vessel. A soln. contg. glycerol monooleate, nonactin (ionophore), and tetradecane was added to the electrode, the electrode was rinsed with saline soln., and urease was nonspecifically bound to the lipid membrane surface. On the addn. of urea, the impedance of the

Page 41

urease/ion selective electrode dropped more than that of the control (identical electrode lacking urease). Synthesis of membrane spanning lipids is described.

IT 156398-50-4 156398-51-5

RL: ANST (Analytical study)

(in prepn. of linker lipid for attaching ionophore-contg. membrane to electrode)

IT 156370-83-1P 156370-84-2P 156370-85-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as membrane-spanning lipid for ionophores-contg. sensor
 membrane)

L21 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1990:115305 HCAPLUS

DOCUMENT NUMBER:

112:115305

TITLE:

Receptor membranes for bisensor devices

INVENTOR(S):

Cornell, Bruce Andrew; Braach-Maksvytis, Vijoleta

Lucija Bronislava

PATENT ASSIGNEE(S):

Commonwealth Scientific and Industrial Research

Organization, Australia PCT Int. Appl., 40 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English 2

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8901159	A1	19890209	WO 1988-AU273	19880727
	CH, DE	, FR, GB,	IT, LU, NL, SE	10000707
AU 8821279 AU 617687	A1 B2	19890301 19911205	AU 1988-21279	19880727
EP 382736 EP 382736	A1 B1	19900822 19941102	EP 1988-907164	19880727
R: AT, BE,	CH, DE		IT, LI, LU, NL, SE	19880727
JP 03503209 CA 1335879	T2 A1	19910718 19950613		19880727
US 5436170	A	19950725	US 1990-473932 AU 1987-3346	19900125 19870727
PRIORITY APPLN. INFO	· •		AU 1987-3348	19870727
,	•		AU 1987-3453 AU 1987-4478	19870731 19870921
			WO 1988-AU273	19880727

Amembrane comprising a closely packed array of self-assembling amphiphilic mols. is characterized in that it incorporates ion channels, and/or at least a proportion of the self-assembling mols. comprise a receptor mol. conjugated with a supporting entity. The ion channel is selected from peptides capable of forming helices and aggregates thereof, coronands, cryptands, podands, or combinations thereof. In the amphiphilic mols. comprising a receptor mol. conjugated with a supporting entity, the receptor mol. has a receptor site and is Igs, antibodies, antibody fragments, dyes, enzymes, or lectins. The supporting entity is a lipid head group, a hydrocarbon chain(s), a cross-linkable mol., or a membrane protein. The supporting entity is attached to the receptor mol. at an end remote from the receptor site. In preferred embodiments the ion channel is gramicidin A, and is preferably gated. Such membranes may be used in the formation

of sensing devices. A lipid gramicidin surface was prepd. on a Pd-coated glass electrode. The 1st monolayer contd. dodecanethiol:gramicidin (30:1) and the 2nd monolayer contd. 1-0-[11-(p-vinylphenoxy)undecanoyl]-2-0octadecyl-3-O-acetoylglycerol (prepn. given): gramicidin R (prepd. by reacting gramicidin, 11-chloro-3,6,9-trioxaundec-1-yl succinate, dicyclohexyldimide, and diethylaminopyridine) (100:1). The electrode was then incubated in an Fab soln. contg. Fab from 2 monoclonal antibodies to 2 distinct sites on human chorionic gonadotropin (hCG). HCG at 0.96 ng/mL in 0.1M NaCl gave an impedance of 106.20 .OMEGA. at 10 mHz corresponding to 4.8 .times. 104 conducting gramicidin channels, measured at 1 mHz. Before hCG, the impedance was 106.15 .OMEGA. at 10 mHz arising from 5.9 .times. 104 conducting gramicidin channels at 1 mHz.

124804-88-2P 124804-89-3P 124804-90-6P TT RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, in prepn. of receptor membrane for biosensor)

L21 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1989:453651 HCAPLUS

DOCUMENT NUMBER:

111:53651

TITLE:

Diethylene glycol distearate as an embedding medium

for immunofluorescence microscopy

AUTHOR(S):

Valdimarsson, Gunnar; Huebner, Erwin

CORPORATE SOURCE:

Dep. Zool., Univ. Manitoba, Winnipeg, MB, R3T 2T2,

Can.

SOURCE:

Biochemistry and Cell Biology (1989), 67(4-5), 242-5

CODEN: BCBIEQ; ISSN: 0829-8211

DOCUMENT TYPE:

Journal English

LANGUAGE:

Diethylene glycol distearate was tested for indirect immunofluorescence microscopy. Rhodnius ovarioles were embedded in diethylene glycol distearate, sectioned at 1-2 .mu.m, mounted onto coverslips, and stained with antitubulin antibodies followed by fluorescein-conjugated secondary antibodies. Flat, brightly stained sections with low background fluorescence were obtained routinely, suggesting that diethylene glycol diesterate may be generally applicable for immunofluorescence localization

of cytoskeletal proteins in tissues. 109-30-8, Diethyleneglycol distearate IT

RL: ANST (Analytical study)

(embedding medium, for insect tissues for immunofluorescent staining)

=> select hit rn 121 1-12 E78 THROUGH E106 ASSIGNED

=> fil reg FILE 'REGISTRY' ENTERED AT 15:43:35 ON 10 APR 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

9 APR 2003 HIGHEST RN 502545-60-0 STRUCTURE FILE UPDATES: 9 APR 2003 HIGHEST RN 502545-60-0 DICTIONARY FILE UPDATES:

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when

Russel 09/018,879 Page 43

conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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STN Files:

CA, CAPLUS

LC

PAGE 1-A

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PAGE 1-B

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:149948

L23 ANSWER 5 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN 477775-74-9 REGISTRY

CN Octadecanoic acid, 25-phenyl-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl

ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C41 H74 O10

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A

PAGE 1-B

-
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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1962 TO DATE) 6 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:29120

REFERENCE 2: 138:16637

REFERENCE 3: 138:16636

REFERENCE 4: 138:16621

L23 ANSWER 10 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN 352536-12-0 REGISTRY

CN Glycine, N-[[(3.beta.)-cholest-5-en-3-yloxy]carbonyl]-L-homoseryl-4-[2-(2-

aminoethoxy)ethoxy]-4-oxobutanoyl-N-methyl- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C43 H71 N3 O10

SR CA

LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1962 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:167010

L23 ANSWER 15 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN **331968-77-5** REGISTRY

CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-[2-oxo-2-[2-(2-pyridinyldithio)ethoxy]ethoxy]- (9CI) (CA INDEX NAME)

MF (C2 H4 O)n C10 H13 N O3 S2

CI PMS

PCT Polyether

SR CA

LC STN Files: CA, CAPLUS, USPATZ, USPATFULL

$$S-S-CH_2-CH_2-O-C-CH_2-O-CH_2-CH_2-O-D_n$$
 Me

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:266736

L23 ANSWER 20 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN **321904-99-8** REGISTRY

CN Poly(oxy-1,2-ethanediyl), .alpha.-(cyanoacetyl)-.omega.-[2-[[(1,1-dimethylethoxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

DR 321905-01-5

MF (C2 H4 O)n C10 H16 N2 O4

CI PMS, COM

PCT Polyether

SR CA

LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:136545

L23 ANSWER 25 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN **262857-77-2** REGISTRY

CN Carbonic acid, 2-(2-hydroxyethoxy)ethyl 2-(trimethylsilyl)ethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C10 H22 O5 Si

SR CA

LC STN Files: CA, CAPLUS, CASREACT

O || Me3Si-CH2-CH2-O-C-O-CH2-CH2-O-CH2-OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERÈNCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:251326

L23 ANSWER 30 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN **259228-98-3** REGISTRY

CN Hexadecanoic acid, 2-[2-[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]e thoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C27 H47 N O9

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 5 REFERENCES IN FILE CA (1962 TO DATE)
- 4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 6 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:29120

REFERENCE 2: 138:16637

REFERENCE 3: 138:16636

REFERENCE 4: 138:16621

REFERENCE 5: 132:185416

L23 ANSWER 35 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN 229645-50-5 REGISTRY

CN 3,6,9,12-Tetraoxatetradecanoic acid, 14-amino-, ethyl ester (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Ethyl 14-amino-3, 6, 9, 12-tetraoxatetradecanoate

FS 3D CONCORD

MF C12 H25 N O6

CI COM

Russel 09/018,879

Page 49

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:313453

REFERENCE 2: 132:122950

REFERENCE 3: 131:88341

L23 ANSWER 40 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN 221630-74-6 REGISTRY

CN Poly(oxy-1,2-ethanediy1), .alpha.,.alpha.'-(1-oxo-1,2-ethanediy1)bis[.omega.-hydroxy-(9CI) (CA INDEX NAME)

DR 224444-75-1

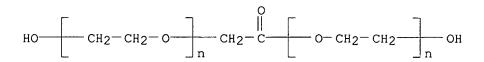
MF (C2 H4 O)n (C2 H4 O)n C2 H4 O3

CI PMS

PCT Polyether

SR CA

LC STN Files: CA, CAPLUS, USPATFULL



4 REFERENCES IN FILE CA (1962 TO DATE)

4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:33720

REFERENCE 2: 134:300865

REFERENCE 3: 130:357165

REFERENCE 4: 130:253129

L23 ANSWER 45 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN 214626-71-8 REGISTRY

CN 14,17,20,23,26,29,32-Heptaoxa-2-thiatetratriacontan-34-oic acid, 1,1,1-triphenyl-, ethyl ester (9CI) (CA INDEX NAME)

MF C46 H68 O9 S

SR CA

LC STN Files: CA, CAPLUS

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$$-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-S-CPh_3$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE) 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 129:302868

L23 ANSWER 50 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN **204652-44-8** REGISTRY

CN Cholest-5-en-3-ol (3.beta.)-, 13-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]-13-oxo-3,6,9,12-tetraoxatridec-1-yl butanedioate (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C50 H71 N O11

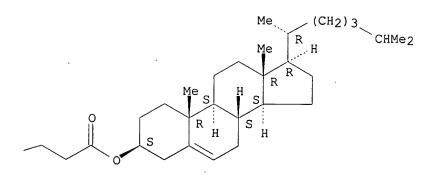
SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:157549

REFERENCE 2: 133:168250

REFERENCE 3: 128:230562

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RN 183872-90-4 REGISTRY

CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.OMEGA.-hydroxy-, ether with (OC-6-23)-bis(1,2-ethanediolato-.kappa.O)[8,13,24,29-tetraphenyl-33H,35H-dibenzo[b,1]dinaphtho[2,3-g:2',3'-q]porphyrazinato(2-)-.kappa.N33,.kappa.N34,.kappa.N35,.kappa.N36]silicon (2:1), mono[3-(acetylthio)propanoate] (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.OMEGA.-hydroxy-, ether with (OC-6-23)-bis(1,2-ethanediolato-0)[8,13,24,29-tetraphenyl-33H,35H-dibenzo[b,1]dinaphtho[2,3-g:2',3'-q]porphyrazinato(2-)-N33,N34,N35,N36]silicon (2:1), mono[3-(acetylthio)propanoate]

MF (C2 H4 O)n (C2 H4 O)n C73 H52 N8 O6 S Si

CI CCS, PMS

PCT Polyether

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

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$$-CH_2-O$$
 $-CH_2-CH_2-O$
 $-CH_2-CH_2-SAC$
 $-CH_2-CH_2-SAC$

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:78227

REFERENCE 2: 126:33023

L23 ANSWER 60 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN **156370-85-3** REGISTRY

CN 5,8,11,14,17-Pentaoxaheneicosanedioic acid, 4,18-dioxo-,
3-[[16-[4-[[43-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-y1)-22,25,32,39tetraoxo-19-[(3,7,11,15-tetramethylhexadecyl)oxy]-17,21-dioxa-24,31,38triazatritetracont-1-yl]oxy]phenoxy]hexadecyl]oxy]-2-[(3,7,11,15tetramethylhexadecyl)oxy]propyl 14-phenyl-3,6,9-trioxa-12,13dithiatetradec-1-yl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Thieno[3,4-d]imidazole, 5,8,11,14,17-pentaoxaheneicosanedioic acid deriv.

FS 3D CONCORD

MF C139 H247 N5 O26 S3

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

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$$\begin{array}{c} \text{O} \\ \text{Ph-CH}_2\text{--}\text{S--S-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text$$

PAGE 1-B

PAGE 1-D

$$-$$
 (CH₂)₃-CHMe₂

PAGE 2-C

PAGE 3-C

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 121:77743

L23 ANSWER 65 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN 149299-81-0 REGISTRY

CN Glycine, N-[N-[N-[(benzoylthio)acetyl]glycyl]glycyl]-,

2-[2-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethoxy]ethoxy]ethyl ester

(9CI) (CA INDEX NAME)

MF C25 H30 N4 O12 S

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

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PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 119:134568

REFERENCE 2: 119:103320

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Searched by M. Smith

RN 139729-26-3 REGISTRY CN Poly(oxy-1,2-ethanediyl), .alpha.-(2-chloroethyl)-.omega.-(2-ethoxy-2oxoethoxy) - (9CI) (CA INDEX NAME) MF (C2 H4 O)n C6 H11 C1 O3 CI PMS PCT Polyether SR CA LCSTN Files: CA, CAPLUS 1 REFERENCES IN FILE CA (1962 TO DATE) 1 REFERENCES IN FILE CAPLUS (1962 TO DATE) REFERENCE 1: 116:152389 L23 ANSWER 75 OF 87 REGISTRY COPYRIGHT 2003 ACS 131029-43-1 REGISTRY RN CN Acetic acid, [2-(triphenylmethoxy)ethoxy]-, ethyl ester (9CI) (CA INDEX NAME) OTHER NAMES: CN Ethyl [2-(triphenylmethoxy)ethoxy]acetate MFC25 H26 O4 SR LC STN Files: CA, CAPLUS, USPATFULL 0 EtO-C-CH2-O-CH2-CH2-O-CPh3 **PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT** 3 REFERENCES IN FILE CA (1962 TO DATE) 3 REFERENCES IN FILE CAPLUS (1962 TO DATE) 1: 131:272145 REFERENCE REFERENCE 2: 127:121636 REFERENCE 3: 114:23805 L23 ANSWER 80 OF 87 REGISTRY COPYRIGHT 2003 ACS RN **113395-48-5** REGISTRY CN Hexadecanoic acid, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME) FS 3D CONCORD MF C23 H46 O5 SR CA LC STN Files: CA, CAPLUS

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1962 TO DATE)
- 3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 108:114393

L23 ANSWER 85 OF 87 REGISTRY COPYRIGHT 2003 ACS

RN 10233-14-4 REGISTRY

CN 9-Octadecenoic acid (9Z)-, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

OTHER. CA INDEX NAMES:

CN 9-Octadecenoic acid (Z)-, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester

CN Oleic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (8CI)

CN Triethylene glycol, monooleate

OTHER NAMES:

CN Motricol

CN Triethylene glycol oleate

FS STEREOSEARCH

DR 240111-08-4

MF C24 H46 O5

LC STN Files: CA, CAPLUS, CHEMCATS, CHEMLIST, TOXCENTER, USPATFULL Other Sources: EINECS**, NDSL**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.

Me
$$(CH_2)$$
 7 Z (CH_2) 7 O O O O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 6 REFERENCES IN FILE CA (1962 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 6 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:76386

REFERENCE 2: 119:228494

REFERENCE 3: 96:87439

REFERENCE 4: 96:57579

REFERENCE 5: 81:96326

REFERENCE 6: 79:94338

L23 ANSWER 87 OF 87 REGISTRY COPYRIGHT 2003 ACS

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109-30-8 REGISTRY
RN
    Octadecanoic acid, oxydi-2,1-ethanediyl ester (9CI) (CA INDEX NAME)
CN
OTHER CA INDEX NAMES:
CN Diethylene glycol, distearate (8CI)
     Stearic acid, oxydiethylene ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN
     Oxydiethylene stearate
CN
     Witconol CAD
     3D CONCORD
FS
MF
    C40 H78 O5
CI
    COM
LC
     STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST,
       CSCHEM, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 43 REFERENCES IN FILE CA (1962 TO DATE)
- 43 REFERENCES IN FILE CAPLUS (1962 TO DATE) 2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:314759

REFERENCE 2: 131:279317

REFERENCE 3: 129:335477

REFERENCE 4: 129:130325

REFERENCE 5: 129:75411

REFERENCE 6: 128:330159

REFERENCE 7: 128:53045

REFERENCE 8: 124:346616

REFERENCE 9: 124:185402

REFERENCE 10: 121:249934